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THE EVALUATION OF A RELEVANT APPROACH TO CLINICAL PHARMACY

by

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ABSTRACT

Problems relative to the establishment of effective and relevant clinical pharmacy services were recognized during the residency component of the author's graduate program in Clinical Pharmacy. Since drug information -- its collection, selection, evaluation and communication -- is considered the basis of clinical pharmacy, problems related to it were investigated.

Literature, reporting drug interactions, was evaluated and it was demonstrated that many limitations and shortcomings are present in the current literature.

In a retrospective medical records survey it was found that several drugs are prescribed together in practice and often in the same combinations which, according to the literature, have the potential for interacting and altering each others effects.

Finally a comparative evaluation of the time required to screen drug therapy for potential interactions was undertaken. The study was done in two hospitals, using a centralized approach in one and a decentralized one in the other. From the point of view of time requirements, the centralized system was apparently the more efficient of the two approaches.

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INTRODUCTION

The concept of clinical pharmacy has widespread acceptance but it has different meanings for different people. Indeed, Francke suggests that there is a need for two definitions of clinical pharmacy-- "one as a clinical component of an educational experience and the other as a mode of professional practice" (1). The Curriculum Committee of the American Association of Colleges of Pharmacy has defined clinical pharmacy as "that area within the pharmaceutical curriculum which deals with patient care with emphasis on drug therapy" (2). Francke has modified this definition and says, "Educationally, clinical pharmacy may be defined as a concept which considers the treatment and care of patients by members of the health team in the presence of pharmacy students with particular emphasis on the safe and appropriate use of drugs" (1). These statements reflect the necessity for teaching students how to identify the need for and the application of their extensive knowledge of drug products as related to drug usage.

"The practice of clinical pharmacy maintains the same principal concept but here the pharmacist replaces the student and utilizes professional judgment based on his theoretical knowledge while working with members of the health care team to foster the safe and appropriate use of drugs in patients" (1).

Tyler states that "In practice, it is patient-oriented and includes not only the dispensing of required medication, but also advising the patient on the proper use of all medications, both prescribed and patient-selected. It also utilizes the pharmacist as an information source for members of the medical and other health professions on all matters pertaining to drugs and their dosage forms" (3).

In essence, clinical pharmacy is a patient-centered pharmacy practice and clinical pharmacy education prepares the student to function in this capacity in any environment.

The efficacy and safety of drug use are as much a professional obligation to the ambulatory patient as they are to the institutionalized one. Thus, there is no need to differentiate amongst the functions performed by a professional pharmacist in a hospital, in a clinic dispensary or in a community store. The most generally accepted objectives of clinical pharmacy, applicable to both the community and the institutional pharmacists, have been clearly outlined by Parks (4) as follows:

> "1. maintenance of patient drug records of both Rx legend and OTC drugs for the benefit of both the patient and the physician:
>
> 2. the monitoring of drug therapy for possible adverse drug reactions, of drug-drug, drug-food, and drug-laboratory test interactions; this includes multiple prescriptions from the same physician for the same patient, single prescriptions from more than one physician for the same patient and interaction of self-medication drugs with prescribed drugs.
>
> 3. professional advice to the patient on the proper use of all drugs, both prescribed and self-selected, their possible side effects, contraindications, storage conditions, etc.
>
> 4. information source to the physician for reliable value judgments on the choice of drugs and the comparative therapeutic merits of drugs.
>
> 5. orientation of the patient to the health care system, including information on where and how he enters the system and the benefits he can expect from it."

It must be recognized that many pharmacists in all types of pharmacy practice are attempting to fulfil some or all of these objectives and that their success in this attempt ranges from a low level to a very admirable level. "Since the concept of clinical pharmacy is everywhere in the developmental stage, the difference in practice is mainly in the approach and level of sophistication" (5). The approach and level of sophistication are dependent upon the pharmacist's interpretation of clinical pharmacy and upon his experience,

education and motivation, as well as upon the unique characteristics of his site of practice which may necessitate a different emphasis. For example, in hospitals the approach to providing pharmacy services varies from hospital to hospital. A multitude of variables such as the size of the hospital, the nature of the hospital-- that is, whether it is privately-owned or community-owned, and whether it is an active-treatment facility or an extended-care facility -- the type of drug distribution system employed and other factors influence the nature and sophistication of pharmacy services provided.

Because of the many variables in pharmacy practices, a universal formula cannot be designed and prescribed for the implementation of clinical pharmacy practice. There are many techniques frequently promoted for the surveillance of drug usage and for the communication of drug information; however, from personal experience in the inpatient area of a teaching hospital, many of these are not always economically feasible as a service function (6). There is a need for the analysis of these techniques and for the design of a relevant approach for providing adequate clinical pharmacy services in the inpatient area of hospitals (7).

What are the potential problems generated by inadequate drug information? What is the clinical significance of these problems? How can pharmacy effectively influence the solution of these problems? These are a few of the types of questions that require answering in order that a relevant approach can be developed.

II. LITERATURE AND RESIDENCY REVIEW

Drug information is the basis of clinical pharmacy. Without adequate and relevant knowledge about drugs the pharmacist cannot contribute in the promotion of safe and effective drug therapy. To attain this end the pharmacist must be constantly involved in the selection, evaluation, compilation and communication of relevant and accurate drug information.

There are several methods by which the pharmacist can participate in the communication of drug information. The method which he selects will depend on whether he is communicating with the patient or with health care personnel and it will depend on whether the pharmacist is collecting or disseminating information.

The concept of a pharmacist providing drug information is not new. He has always provided the physician and nurse with the traditional type of information about drug sources, dosages, formulation and cost (8,9). This is information that the pharmacist can provide without knowledge of the physical, chemical or biological behavior of drugs (9) and without knowledge about the clinical background of a patient. The pharmacist can also provide a more sophisticated type of information which requires the application of his knowledge of the physical, chemical and biological properties of drugs to drug usage. These aspects must be considered when answering questions about drugs such as those dealing with compatibility, milliequivalents, the absorption, distribution and fate of drugs in the body, duration of action, side effects and antidotes (9). A great many pharmacists are providing this type of information adequately.

A second type of drug information which some pharmacists are now providing to physicians and other health care personnel as part of clinical pharmacy services, (10,11,12) may be classified as "potential" information.

The pharmacist does not necessarily receive a request for this type of information because the need for it is not readily apparent. Usually, the need for potential drug information is generated only through reviewing the use of drugs, in combination or alone, with respect to the efficacy of drug therapy and other aspects of patient care. The pharmacist can sometimes identify potential drug-related problems while following a patient's drug therapy or during ward rounds and thereby can volunteer information about drug interactions and about dosage requirements in relation to physiologic and physical features as well as food intake and other supportive measures. He can also recognize drugs which interfere with laboratory or other tests, contraindications, precautions and the characteristics of early drug toxicity (13). "To be useful, this information must be both positive and appropriate in the total context of the case" (12). That is, the pharmacist must draw attention to only the significant potential problems of drug therapy and he should propose alternatives for modifying and/or correcting therapy.

To effectively provide the aforementioned types of drug information the pharmacist must have available the required sources of relevant data, the proper background to evaluate the significance of such data, a mechanism to identify the needs for information and a method of efficient communications to satisfy this need. Significant progress has been made in each of these areas with respect to the first type or traditional information. The following discussion represents such progress as reported in the literature and as experienced during the residency portion of the current graduate program. Much effort is still required, however, before pharmacy can fulfil the needs of potential drug information. This fulfilment is the primary objective of Clinical Pharmacy. An evaluation of some aspects of this objective is the primary purpose of the experimental approach of the present study.

A. SOURCES OF DRUG INFORMATION

To provide the accurate and relevant traditional and potential drug information described earlier, the pharmacist requires access to comprehensive and reliable sources of information. A drug information center is a valuable resource for this purpose. It derives information primarily from pharmaceutical and medical sources of a varied nature (14,15,16,8) and in reciprocal fashion communicates this information when and where it is needed to all health professionals.

Drug information centers evolved in the 1960's (17,18) in an attempt to bridge the "information gap" (19). The exponential growth of biomedical knowledge challenged and still challenges each of the health professions to be informed and to introduce this new knowledge into the therapeutic management of the patient (8). "From its beginning the operation of a Drug Information Center has embraced the concepts that it is indeed possible to bring organization to the methods through which a pharmacist can disseminate drug information and that by providing this information a meaningful service could be made available to the medical and paramedical professions" (8).

A drug information center is expected to contain all relevant information on drugs and drug usage with the facility for efficient input and output of data. Product information forms such as the "ASHP Drug Product Information Form" (20) or such as the adapted version,developed as a residency project, (see Appendix I) can be utilized by the center to provide the most commonly required data about drugs. In addition, drug information centers can serve as a source of information about current drug usage trends arising out of the drug experiences in each hospital. For the most part, this information is still lying dormant in medical records, but there is a growing interest to untap and to utilize this data.

The foundation of drug information services is literature, published and unpublished (21). "Drug literature is growing rapidly in size. It is also increasingly complex, that is, interdisciplinary and interprofessional in nature. Thus, drug information 'sprawls across' many professional journals of the most varied types" (22). This means that required information must be selected and collected from a multitude of sources. Furthermore, "competent evaluation of the masses of drug information is particularly necessary" (22) in order that valid and useful drug information can be made available. Although there are some guides for the evaluation of drug literature and drug trials such as one outlined by Mahon and Daniel (23) or such as the two-volume series, entitled "Clinical Pharmacology", (24) the task of interpreting and evaluating drug literature requires skill and judgment based on a broad biological and physicochemical background and experience.

The growing demands for drug information, the increasing number of sources of drug information and the increasing complexity of evaluating drug information stress the importance of well-trained and competent pharmacists in this area. Many current pharmacy curricula produce product-oriented pharmacists who can satisfactorily provide traditional drug information. Unfortunately such curricula do not adequately prepare the pharmacist to cope with the aforementioned problems and to provide potential drug information. A patient-orientation is also required to meet these needs. This includes familiarizing the pharmacist with laboratory tests, disease conditions and medical terminology. Training in the biological and clinical application of drug therapy as well as in the chemical and physical properties of drugs enables the pharmacist to evaluate and to interpret more adequately the drug information in the context of the patient's condition. Clinical Pharmacy education is attempting to achieve this objective.

B. REVIEWING THE NEEDS FOR DRUG INFORMATION

Although the following presentation reflects the general needs for drug information in society, specific attention will be given to the needs based on institutional patient care.

1. Patient Admission Medication History

Medical doctors recognize the need for medication histories. In his article "Ill-Health Due to Drugs", Dr. Wilson states, "It cannot be too strongly emphasized that no clinical history is complete without a list of drugs taken during the previous six months" (25). A drug history provides the physician with important aspects about the patient because drugs can have widespread effects upon the body. Some drugs can cause adverse effects mimicking disease states. For example, chlorpromazine in high doses can produce a parkinsonian syndrome (26). Some drugs can have prolonged effects on the body. For example, following the withdrawal of glucocorticoid therapy (which causes reduction of adrenocortical function) a period of six months or more may be required for the return of the maximum functioning capacity of the adrenal that may be required during stress (27,28). These are but two examples where knowledge of the patient's drug history enables the physician to plan rational therapy. An awareness of the patient's past drugs, of how closely he has followed his past course of treatment and of any adverse drug reactions or allergic responses decreases the risk of inappropriate therapy for that patient. Also, the drug history insures that a patient will be maintained on any critical drug regimen after his admission to the hospital.

Until recently pharmacists were not at all involved in this function of eliciting a drug history. In fact, it appears that drug histories were not routinely determined by any personnel. In a survey (29) conducted by the Joint Medicolegal Education Committee of the California Hospital Association and California Medical Association in member

hospitals, it was found that only 38.5% of 332 hospitals required information about recent use of certain drugs. The personnel employed to obtain this information ranged from physicians to ward clerks and nursing aides. No mention of a pharmacist performing this function was made.

The status of drug histories was reviewed briefly in two hospitals in the present study. In a large teaching hospital 29 out of 30 patients had been asked about their medication history by the medical historian and the admitting nurse. In a non-teaching hospital, only 15 out of 30 patients had evidence of a medication history in their charts. In both institutions all of the patients were queried about allergies.

Many of the medication histories taken in both of the institutions were incomplete: only prescription drugs were considered; usage regimens, including strength, dosage and duration of use were unavailable; and occasionally drugs were not positively identified, e.g., a red pill for the heart. Unless the patient is asked specific questions about his drug usage habits much information will be lost. Patients medicate themselves liberally with over-the-counter preparations (which they do not consider to be drugs); women use oral contraceptives which often they do not consider to be drugs; people sometimes use their neighbor's medications. The question "What drugs are you taking?" does not necessarily ensure an accurate nor a complete drug history.

There is a need for more adequate drug histories (30,31,32,33). In some hospitals, pharmacists are functioning in this capacity. During the interview, the patient's past and current medication regimen of prescribed and non-prescribed drugs is sought. The dosage, duration of use, reason for discontinuation and knowledge of whether the use is continuous or intermittent are desirable information. Also the patient's known allergies, adverse reactions to drugs, significant illnesses and any social or behavioral

problems that are important to the patient's drug therapy are included in the drug history (5,11,31,32,34).

This information is then made available to the physician and other health care personnel usually by inclusion in the patient's chart so that it can be integrated with other medical history data obtained (33,35).

The drug history is usually obtained after the physician's admitting examination. This allows the pharmacist to review the patient's chart and to approach the patient with some understanding of his condition. Thus, the pharmacist has an idea of what type of questions to ask and is consequently able to elicit a more complete drug history.

In a pilot project undertaken at Providence Hospital, a pre-admission drug history,obtained through a telephone interview by a pharmacist on the evening prior to the patient's admission,proved equally as satisfactory as a personal interview on the day of admission (36).

Studies have been conducted showing that a pharmacist can serve as an effective interviewer in determining the past medication history of patients admitted to hospitals (31,33,37). Wilson & Kabat (38) compared the drug histories elicited by pharmacists and by physicians and found that only 57% of the medications found by the pharmacist were recorded by the physician. Although the physician recorded 70% of the patient's prescribed medications, he recorded only 37% of the non-prescribed medications found by the pharmacist. Because of their familiarity with non-legend drugs as well as legend ones, pharmacists can develop a more complete drug usage picture.

Furthermore, because of their familiarity with drug products, pharmacists can more readily identify unlabelled ones. In Wilson and Kabat's study, physicians were able to identify specific drug products which the patients were taking 77% of the time compared with an 86% identification

rate for the pharmacist (38). In addition to identification by sight, the pharmacist can perform the identification task by tracing a prescription number to the pharmacy from which it was dispensed, by identifying code numbers on some of the solid dosage forms, and by using various identification charts and guides provided by the manufacturers and one devised by the American Medical Association (39).

Each pharmacist can design and develop his own identification guide. One that was designed as a residency project during the current program for the degree of Master of Hospital Pharmacy utilizes coin collectors' material. It is an adaptation of a display system developed by the Massachusetts General Hospital Pharmacy Department (41). The identification display consists of a cardboard frame with transparent windows in which the tablets or capsules are mounted. The mount is inserted into a transparent compartmented page. Alongside each mount is a brief typewritten description of the product, including the trade name, the ingredients and their quantities, the manufacturer and the therapeutic classification. The products are categorized, both, by color and by therapeutic use: that is, all dosage forms of one color are grouped together regardless of therapeutic use and all products of a particular therapeutic use are grouped together in another classification regardless of color. The two classifications are kept in separate sets of three-ring notebooks and an attempt to identify a product can be made on the basis of the knowledge of its color or its therapeutic use. (See Appendices II and III). This product identification system is currently being employed and evaluated.

The pharmacist, however, is not without difficulties in obtaining an accurate and complete drug history (33,34). Some patients are uncooperative. Some are confused. Sometimes the patient is absent from his room. Sometimes the patient is being treated or interviewed by another health

care person. Sometimes the patient is too ill to be disturbed. Sometimes the patient pours all of his medications into one container or loses the labels. Sometimes the patient may receive medications in a doctor's office or another hospital and have no idea of what they are. Sometimes language is a barrier.

To obtain an in-depth medication history in view of the aforementioned difficulties is a time consuming effort. McHale and Canada found that the average time required for interviewing patients was 4.15 minutes per patient (33). Wilson and Kabat (38) discovered that the average interview required just over nine minutes, however an additional 24 minutes per patient were required to reach the patient care area, to locate a specific patient and to identify his drug products. Other pharmacists have estimated longer periods (5,30). The author's personal experience, using a preprinted form, (See Appendix IV) showed that about 10 - 12 minutes were required just for the interview once the patient was located.

The previous discussion exemplifies the pharmacist's potential contribution in obtaining a medical history; however, on the basis of the time requirement, it does not seem feasible that the pharmacist interview each newly admitted patient. It seems reasonable to assume that the desired objectives may best be achieved through one or more of the following procedures.

Each patient, being electively admitted, might have forwarded to him prior to his admission an adequately designed medication history form, similar to the one designed as a residency project (see Appendix IV). Upon admission the completed form could be forwarded to the pharmacy department where it would be checked for completeness. If the patient had any unidentified drugs, the pharmacist would identify them. If there were any discrepancies in the information provided by the patient, the pharmacist would interview

the patient in the hospital. In effect, the completed medication history form would serve as a screening agent to identify those patients requiring interviews.

Alternatively, the admissions department personnel might be trained to screen all patients to identify those most likely to have drug-related problems. In addition to the routine admission patient data, patients could be asked if they have allergies, if they are currently taking medications and if they have their medications with them. This admissions information on each patient would be forwarded to the pharmacy. The pharmacist would then interview those patients with allergies or those taking medicines prior to admission since these patients seem to develop drug-related problems (42). This system of screening patients for a drug/chemical interview is being evaluated in Peralta Hospital in Oakland, California (42).

A third possibility that might be feasible in the future would be to forward the patient's family record plans, maintained in community pharmacies, to the hospital upon the patient's admission. This would yield a comprehensive history of all prescribed and self-selected medications which the patient was taking prior to admission with no demands upon hospital personnel. However, because of the public's present promiscuous drug purchasing habits this suggestion is not currently realistic.

2. Patient Discharge Interview

The discharge interview provides the pharmacist with another opportunity to communicate with the patient about drugs. During this contact the patient or responsible adult is advised on the correct usage of any medications taken at home. The information which the pharmacist extends to his patients has been discussed by several authors (43, 44,45,46) and is summarized in the list prepared by Brand (47):

"1. who the medicine is for

2. what the medicine is to be used for or its general classification

3. the name of the medicine

4. how to use the medicine

5. when to use the medicine

6. how long to use the medicine

7. maximum amount that may be taken safely in one day

8. the side reactions he (the patient) might expect

9. what to avoid in activities such as driving, working machinery, eating, drinking and taking other drugs

10. special storage and special handling of the medicine."

In giving this information to the patient, Brand cautions that judgment must be used.

The hospitalized patient does not require as much information about his drug therapy regimen because he usually is not responsible for it. It is handled for him by the physician, pharmacist and nurse. However, once the patient is discharged he must take charge of his own drug treatment. How well the patient self-medicates will depend largely on his understanding and appreciation of his drugs and drug regimen (43,48).

In a discussion about the manner in which patients use medications McCarron (32) presents the following views:

> "Patients have remarkable little insight regarding the proper use of drugs. They medicate themselves according to the latest T.V. ad, or a recommendation of a friend. Wives take medication prescribed for their husbands and vice versa; and people give medicines that have helped them to their friends who seem to have a similar need.
>
> Patients obtain prescriptions from physicians, ask the pharmacist how much each item costs, and readjust their therapy by buying some of the prescribed drugs and not others. Even when patients have all of their prescriptions filled, they often do not comply with the instructions for using them. Some patients buy medicine and do not use it - medicine cabinets

> throughout the country contain unused prescription drugs; others use up a month's supply in a few days. Also many patients do not know how to administer drugs properly. They often misuse certain preparations such as inhalers, nose drops and suppositories.
>
> Medications are not stored adequately or safely at home -- thousands of cases of poisoning by drugs occur each year in children who have ingested their parents medications. Improperly stored or outdated drugs deteriorate and toxic products may be formed."

In keeping with this point of view, Tyler (3) points out that "In this state of ignorance patients often use the drugs in a manner which is not only ineffective but definitely hazardous to health."

Many studies which have been conducted on the self-administration of drug therapy by the public confirm the above opinions. These studies show that, in general, patients are somewhat unreliable when charged with the responsibility of self-administration of their prescribed drugs. A study (49) at Peter Bent Brigham Hospital in Boston, showed that 50% of the patients receiving drugs exhibited some error in taking them. Latiolais and Berry, (50) in their study on outpatients, discovered that 42.8% of the patients sampled were misusing their medications. Almost 40% of the patients interviewed by Wilson and Kabat (38) admitted that they did not utilize prescription drugs as directed by their physician. A trend, observed by many of the investigators (50,51,52), showed that the more medications a patient had prescribed for him, the more likely he was to make an error in using them.

A few studies have been conducted in an attempt to correlate medication errors with patient instruction. Latiolais and Berry (50) found that the patients taking their medications correctly received instructions from their physician on 65.8% of their prescriptions as compared to 38.6% of the group making errors. On the other hand, the pharmacist's verbal review of the dosage regimen

instructions made little difference; patients, taking their medications correctly received the pharmacist's instructions on 69% of their prescriptions, whereas those misusing them, on 66% of their prescriptions. Malahy (51) arrived at comparable findings. Latoilais and Berry (50) and Gelber (53) concluded that approximately one-third of the patients did not understand their instructions, and in a survey in Seattle (46), it was detected that 60% of the outpatients were unaware of special precautions to be followed when taking medications.

It is obvious from these studies that too many patients do not self-medicate properly. These patients give a broad spectrum of excuses for this misuse, ranging from forgetting to finding their prescription too expensive (38). Regardless of what the immediate reason for misuse is, the basic problem is the patient's lack of understanding and appreciation of the proper use of drugs, both, prescribed and non-prescribed.

There is definitely a need to increase the patient's appreciation and respect for drugs. Presently, no one seems to be adequately communicating the importance of this to the patient. The pharmacist is certainly knowledgeable enough about drugs to perform this function (54,55) but his involvement must be more than merely reading aloud the directions on the patient's prescription bottle (50,51).

Before the pharmacist can adequately participate in the education of the patient about his drug therapy, the physician and pharmacist must both have an understanding of what each is doing and of what each expects the other to do to foster safe drug usage habits in the patient. Whatever the pharmacist communicates to the patient must reinforce the patient's confidence in his doctor's selection of drug therapy in addition to ensuring safe and appropriate usage.

At present, many physicians consider patient guidance about prescribed drugs their duty and not the pharmacist's; but there are even more physicians who are not aware that the pharmacist might provide or be able to provide meaningful guidance to the patient (56). Thus, the physician must be made aware of the type of information which the pharmacist can supply to the patient and that he can provide it competently and professionally. Likewise the pharmacist must be made aware of what type of drug information the physician wants and expects his patient to have. The above objectives will not be realized until the physician and pharmacist begin working more closely in recognizing each others needs and capabilities.

The instruction and education of the patient by the pharmacist can best be effected where and when the patient actually obtains his medications for self-administration. Whether it be in a community pharmacy or in a hospital, this allows the pharmacist to make specific reference to each medication which the patient has received. "Instructions (about medications) should be clear and understandable. They should not be so simple that the patient misinterprets them" (32). The pharmacist must be satisfied that the patient has a complete understanding of his drug therapy. Particular attention must be given to parents of sick children, elderly patients with limited activity as well as failing eyesight and memories, and those with chronic conditions that require continued specialized drug therapy (5). The illiterate patient also requires special consideration.

The initiation of supervised self-administered medication programs (57,58,59) for hospitalized patients might be a means by which patients could learn to use their medications correctly. Under the training and supervision of the nursing and pharmacy staffs, the patients would be allowed to self-administer drugs in

preparation for this task upon their discharge. Patients on complex drug therapy or on long-term therapy following discharge would undoubtedly benefit most from such programs. This approach has been introduced and studied in a few hospitals (57,58) and has been considered useful.

In hospitals where patients are supplied with discharge medications, the discharge interview provides an excellent opportunity for the pharmacist to discuss the patient's drugs with him and to inform the patient about proper usage of prescribed and self-selected drugs. A discharge interview is much less meaningful when the patient is not supplied with the discharge medications. In such circumstances, the pharmacist in the community who dispenses the medication to the patient is in the more favorable position to teach the patient about medication usage.

Recent developments indicate that the pharmacist in the community may have increasing opportunity to fulfil this responsibility. There is a growing trend by these pharmacists to maintain patient or family drug record plans (60). These plans provide a mechanism for recording in one place, all of the drugs, prescribed and self-selected, which the patient obtains in that pharmacy. Pertinent patient information, such as allergies or adverse drug reactions, is also recorded. With the aid of this system the pharmacist can more effectively participate in assuring therapeutic appropriateness for his patient. For example, he may discourage a patient from purchasing an over-the-counter preparation which is contraindicated with a prescribed medication which the patient has at home. Or he may use the plan to prevent duplication of therapy from different physicians. It seems apparent that when all community pharmacies adopt the family drug record systems and that when the public changes its casual drug purchasing habits, a greater degree of protection will be offered to the patient.

An ideal situation might be projected whereby upon admission to a hospital, a patient's drug record plan would be forwarded there. This would provide a complete medication history without the need for hospital personnel to establish it. Upon discharge, a list of the medications which the patient received in the hospital would be sent to the patient's community pharmacy and thereby a continuous medication record could be maintained. Problems, including the legality of transferring such information and the physician-patient confidentiality, would require consideration.

Since the pharmacist is the last health care personnel in the process by which an ambulant patient receives his medication, he must insure that the patient has received the correct drug in the correct dosage with the correct instructions and that the patient understands how to use it correctly and safely. Regardless, whether the pharmacist in the hospital or in the community fulfils the above obligations, it is apparent that pharmacy must assume a larger responsibility in influencing the proper and safe use of drugs at this stage.

3. Physicians' Needs

"It is the physician who . . . must make the decision on which drug or drugs to prescribe" (61). It is his responsibility to make the most appropriate or rational selection of a drug. "Rational prescribing is obviously the result of judgement on many points -- the safety and efficacy of the drug for the clinical problem at hand, the advantages or disadvantages of alternative forms of therapy, the most appropriate dosage form, the length and intensity of treatment, the possible side effects or adverse reactions, and the possibility of drug interaction" (62). Apparently the most appropriate decision is not always made since the Task Force on Prescription Drugs (61) and other studies (63,64) indicate that irrational prescribing of drugs is indeed a problem. Rational prescribing necessitates that the physician has adequate relevant and accurate information upon which to make his decision. Although the physician is faced with a barrage of advice, information, guidance and promotion from detail men, advertisements, medical articles, pamphlets and throw-away journals about competetive and duplicate products, the Task Force on Prescription Drugs concluded that many and perhaps most physicians do not have adequate access to complete and objective information on prescription drugs (61). It is in the provision of such information that pharmacy can and must make a more effective and less biased contribution.

Studies have been conducted on the sources of drug information used by physicians. Winnick (65) found that medical journals, medical representatives, direct mail advertising and pharmacists, in that order, were considered by physicians to be reliable sources of information. Williamson and Kabat (66) found that reference texts such as the "Physicians' Desk Reference,"* medical journals,

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*The "Physicians' Desk Reference" is a collection of monographs of products available in the United States. It is published by Medical Economics Inc., Oradell, N.J., with the cooperation of the manufacturers.

colleagues, medical representatives, pharmacists and package inserts were consulted in that order. Similarly Henley, Tester and Knapp (67) demonstrated that pharmaceutical textbooks such as "Physicians' Desk Reference" and drug salesmen were two important sources of drug information for practitioners.

It is obvious from these studies, that pharmacy has been somewhat under-utilized by the medical profession as a source of information. It is not feasible to suggest that every pharmacist could function as a consultant or advisor to the physician, intern and resident. However, the pharmacist should be able to function as an informant; he should be able to evaluate drugs on the basis of their pharmaceutical properties; he should be able to compare and contrast drugs; and thus, he should be able to provide sufficient data to enable the physician to choose wisely (9,68). In essence the pharmacist should expedite the clinician's acquisition of relevant, timely and reliable information (69).

With experience and with adequate educational prerequisites (69), a pharmacist is capable of developing a consultative capacity (12,70). For example, the Drug Information Analysis Service at the University of California, San Francisco Medical Center which is directed by pharmacists is described as follows (70):

> "The DIAS provides a consultative service to members of the health professions in California. Our service is designed to meet the needs of practitioners who present a drug or therapeutic problem concerning a specific patient. Our staff's experience and knowledge combined with the ability to analyze and interpret drug information form the basis of the entire operation of DIAS. We encourage the utilization of our service for solutions to problems when the solutions are not readily available from the usual sources, e.g., the "Physicians' Desk Reference." These problems involve situations that do not fit classic textbook examples and thus require thought, research and judgement.

> We have evolved these principles of operation as a result of trying to fulfil our basic objectives, i.e., we feel that health professionals, particularly physicians, want consultations, not simply factual data."

However, it is rare, particularly in a large teaching hospital, that a physician will recognize the pharmacist as a potential therapeutic consultant. In the absence of a clinical pharmacologist the physician will turn to one of his colleagues who has a specialty or subspecialty in some field of medicine and who has developed an expertise in the group of drugs which he uses routinely in his field (71). Of greater importance is the fact that this specialist also has clinical experience with these drugs. It is necessary to point out that no pharmacy or clinical pharmacy curriculum is attempting to train the pharmacy student to be a therapeutic consultant -- they are training the student to be a first-class pharmacist capable of providing relevant drug information.

THere probably is a greater need and probably a greater acceptance of drug information from a pharmacist by physicians in smaller community hospitals (71). Often in these hospitals, many of the physicians are general practitioners who treat a multitude of conditions with a multitude of drugs with which they have little opportunity to become thoroughly familiar. In such environments, the physician does not have ready access to a colleague who is a specialist on certain drugs nor does the physician usually have access to a comprehensive medical library. A knowledgeable and motivated pharmacist with access to sources of drug information could provide these physicians with significant and valid information to assist them in their prescribing.

"The physician relies upon the pharmacist to supply advice if called upon. He is not prepared for the pharmacist to volunteer information" (72). The pharmacist must

recognize and appreciate this. He must realize that providing the physician with the "potential" type of drug information, which is usually the volunteering of unsolicited information, is still novel to the physician. "The physician in the past was solely responsible for the health care of his patient. With the many advances in medical care . . . . he is (now learning) to depend on the services of allied health professionals," (72) including pharmacists. To foster the physicians' acceptance and utilization of the pharmacist in extending his role in supplying "potential" drug information, the pharmacist must create a positive atmosphere for collaboration. The pharmacist's personality and the method of handling his knowledge will greatly affect his success in this area.

4. Nurses' Needs

The nurse also uses drug information in her daily activities. In most institutions the nurse is the individual responsible for administering the right drug to the right patient in the right dose at the right time. She is also responsible for observing and reporting the effects of the drug on the patient. Thus, the nurse requires practical information or information categorized as nursing implications.

On the nursing station, the nurses attempt to provide themselves with information about drugs. A formulary, some conversion charts and a desk reference of drugs,such as the CPS* are the most common sources of information. However, nurses consider these inadequate (73,74). Most of the sources available to nurses are drug-oriented rather than patient-oriented or nurse-oriented and while such information is vital, it does not solve the immediate clinical problems confronting the nurse (74).

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*The CPS which is the "Compendium of Pharmaceuticals and Specialties", published by the Canadian Pharmaceutical Association, is a compilation of monographs of Canadian prescription products.

In their study, Benson and Kabat (82) found that the types of information required most often by nurses were: indications for use, drugs stocked, dosage and side effects. The pharmacist can readily provide information of this nature.

To increase patient safety, the nurse requires more than just practical information about administration: she must have an understanding of the basis for the selected drug therapy. Through adequate drug knowledge the nurse is capable of a more rational appraisal of drug therapy and is thus capable of better protection for the patient (74). Here again the pharmacist can acquaint the nurse with relevant pharmacology and therapeutics. "Programs on new drugs, new drug therapy, drug reviews, procedures, laws, policies, metrology, drug distribution, storage, administration, charting and emergency drugs have been shown to facilitate patient care" (164). Nurses recognize their drug information needs and they are anxious to receive current and relevant information in a form which can be readily utilized.

5. Other Needs

Little is said about the drug information needs of the many allied health professionals who are involved in patient care. Sometimes these personnel perform treatments and design regimens without an awareness of how they may affect or may be affected by concomitant drug therapy. Drugs because of their desirable and undesirable physiological effects can either promote or disrupt many of the treatment programs. Unless the health care member is aware of the effects of his patient's drugs, he may attribute the patient's response or lack of it solely to the particular regimen. There are certain precautions or contraindications that patients on some drugs must follow during the course of other therapies. For example, during the early phase of treatment with l-Dopa, many patients experience orthostatic hypotension (75,76). Physiotherapists, giving

treatment to Parkinson's Disease patients on l-Dopa, must have this knowledge in order that they may design therapy which does not require the patient to rise to an upright position too rapidly. Because most of the allied health care personnel -- physiotherapists, dieticians, inhalation therapists, social workers, etc. -- have a poverty of formal training related to drugs, the pharmacist can perform a valuable service in relating drug effects to the functions in which the particular health care individual engages.

The pharmacist's function of "drug-use control" is a composite of all of the individual functions of pharmacy (77). Provision of relevant drug information to the physician, the nurse and the allied health professionals, that is, all those participating in the care of the patient, is a major contribution that the pharmacist can make to the patient's well-being and safety. Each of the health care members has a different interest in the patient's drug therapy program. Each of their needs must be evaluated and satisfied by pharmacy in the most effective way possible.

C. METHODS OF COMMUNICATING DRUG INFORMATION

To communicate drug information effectively, the pharmacist can utilize several methods -- lectures, communications sheets, audiovisual aids, etc. "All of these methods have been used effectively and generally their quality is proportionate to the amount of planning and effort behind them" (17). In selecting a method, the pharmacist must consider the purpose of his communication -- whether it is a response to a specific question or whether it is general information; he must consider the nature and depth of the information to be provided; and he must consider which of the health professionals is going to receive this information. The information also must be communicated in the vocabulary of the health professional (78).

1. Direct Response

The direct response, whether it be verbal or written, is the most frequently utilized method of communicating drug information. A need for extemporaneous information is demonstrated and the question must be processed. "In patient care situations there are no limitations as to the complexities of questions and the time involved in providing the required information to answer these questions varies from a few minutes to several days" (8). Sometimes a verbal response is adequate, but as the complexity of the question increases a written communication is preferable (17,70). Documentation of the facts is important.

During the residency component of the present program a variety of information requests were received. They ranged from "What are the side effects of lithium carbonate" to "We are experiencing difficulty in controlling the prothrombin time of one of our patients. Is it possible that the formulation of the warfarin sodium is causing the problem?" (See Appendix V for handling of questions). Answering the first question was a straightforward listing of data published in the literature. The second question

was a challenge necessitating consultation with a clinical pathologist and a hematology resident. A possible interaction was suspected since other patients receiving the warfarin sodium from the same lot were being adequately controlled. Upon reviewing the patient's drug therapy, it was discovered that the patient was receiving warfarin sodium, nalidixic acid and tolbutamide concomitantly. Recent literature indicated that such a regimen should potentiate the effects of warfarin sodium; however, the opposite findings, as evidenced by the prothrombin times, occurred. The facts from the literature were presented to the physician although no logical explanation for the increased prothrombin time could be established.

These two exercises in drug information illustrate that a direct response containing pertinent information is usually possible although occasions may arise where search of available literature and consultation with specialists will not provide an explanation of a particular phenomenon. There is still a need for a vast amount of research information about drugs and their effects.

2. Rounds

Various rounds are advocated as an opportunity for the pharmacist to provide drug information (5,34,36,79). At these rounds the pharmacist may be queried for both simple information, such as which drugs a particular patient is taking, and for more complex information which he may not be able to provide immediately.

Rounds are an excellent educational experience for the pharmacist (5,6,36,79). It is at rounds where the physicians' evaluations, nurses' observations, and comments about the patient from other health sciences personnel place the objectives and problems of drug therapy in perspective (in the context of the patient's condition). Because of the active exchange of information, rounds improve the understanding of the body of knowledge which

the pharmacist already possesses.

Since the introduction of decentralized pharmacy services and utilization of unit-dose drug distribution systems and pharmacy technicians (4,6,10) the pharmacist has been provided with the mechanism and the time to participate in rounds. However, it should be pointed out that in view of the other responsibilities of the pharmacist and the number of physicians and nurses making rounds, often simultaneously, the pharmacist's routine participation in all rounds is not always realistic nor possible.

Personal experience at medical rounds was most enlightening. The complexities of multiple disease states, further complicated by patients' personalities, illustrated the multitude of factors and difficulties which the physician had to consider when prescribing drugs. Clinical medicine was clearly differentiated from the orderly textbook medicine.

Furthermore, personal experience demonstrated that the physician who was a specialist in a certain field of medicine was also a specialist on the drugs which he commonly prescribed in his practice. As a matter of fact, a specialist was found to be a most useful source of information about the clinical experience with drugs used in his field.

3. Interprofessional Conferences

Interprofessional conferences or seminars can perhaps be described as formal extensions of interprofessional rounds. They allow each of the health professionals present to convey to the other health professionals new knowledge and new developments, occurring in their field, which may be relevant to the others. In this way an appreciation and understanding of new techniques or principles of patient care are fostered.

The organization of successful interprofessional conferences so that the presentations are of general relevance to the entire group requires a great deal of planning and coordination. If improved patient care is the outcome, then the immense effort is well worthwhile.

4. Bulletins and Drug Information Notes

Pharmacy publications aim to improve communications between the pharmacy and the rest of the hospital with regard to drug therapy and drug supply. Since the purpose of the publication is to educate as well as to inform, it serves as a valuable mechanism to provide drug information about new drugs, about a variety of aspects of drug therapy such as adverse drug reactions, and about topics of current interest to the health care staff. As well, the rationale behind the Pharmacy and Therapeutics Committee's recommendations regarding drug selection and drug use can be communicated via this medium. A well-prepared and accurate pharmacy publication makes a meaningful contribution to the drug information needs of the professional staff of a hospital (80,81).

Drug information notes are another mechanism to extend printed, practical information. Drug information notes, containing capsulated drug reviews, are distributed to the nursing staff along with any medication that is sent to the ward. These cards are produced with the main objective of providing the nursing personnel with brief, practical facts pertinent at the time of administration of the drug and at the time of reporting observable effects. The content of the cards is based on the requirements of the nurse (82,83) and usually includes drug names and synonyms, use or category, dose, side effects, cautions and nursing implications, such as how to dilute a drug for injection.

This method of supplying concise and pertinent drug information to the nursing personnel has been utilized

in several hospitals. Greth et al (83) described the use of drug information cards called "Med-Notes"; Mahoney (84) and Barker and Heller (85) have described "Pharmatips"; and Presco and Plein (86) have described medication reference cards called "Med-Refs".

5. Lectures

Lectures are a formal means of transferring information and they can be used to provide drug information to various personnel. They are informational in presenting facts and promoting understanding through clarification and explanation. In preparing a lecture about drugs, it is imperative that the material be tailored to the needs of the audience: the drug information requirements of a physiotherapist are quite distinct from those of a physician. Not only is the selection of the material important, but the vocabulary employed must be that of the audience.

Lectures are a convenient method of presenting information of general interest or need to a large number of people.

The presentation of lectures, during the residency component, to various health care personnel provided a challenge in the preparation of relevant material. For example, lecturing to the physiotherapists about drugs, demanded familiarization with physiotherapy treatments in order to assess what drug effects might enhance or interfere with the physiotherapy procedures.

Lectures are only as effective as the message which they relate. To assist in communicating a message a lecturer can utilize a variety of gimmicks and aids. More and more, audiovisual aids are being used successfully in all forms and all levels of education. Currently, there is a very rich choice of audio-visual aids, which when carefully and thoughtfully applied can be of great use in disseminating drug information. "The teacher's

voice can be extended by sound radio and tape recordings, the blackboard and chalk by slides, film strips, film and television" (87).

Because all of the health personnel are faced with the challenge of a massive amount of new knowledge in their fields, acquiring information about drugs, even though relevant to their practices, is an added burden. Thus, drug information must be presented in a lucid and imaginative manner. Audiovisual aids can be a definite asset in this regard.

The pharmacist disseminating "formal" drug information can make use of a variety of audiovisual presentations, prepared and distributed by pharmaceutical manufacturers or by various hospital departments or he can prepare his own. The preparation of his own audiovisual presentation affords the pharmacist with an opportunity to tailor it to the specific needs of the audience and its development is limited only by his imagination.

To illustrate the usefulness of audiovisual aids in meeting some of the communication needs of pharmacy, a synchronized slide/tape presentation, entitled "Alice's Pharmacological Odyssey" was prepared and presented at a Pharmacy Graduate Student's Seminar (see Appendix VI).

The presentation consisted of slides -- the pathological and clinical ones, acquired from the Medical Photography Department or clinicians, and other slides, drawn or created from magazine pictures,arranged collage style -- synchronized with a commentary recorded on audio tape. Assistance and advice for the preparation was received from medical personnel and the Audio Visual Department.

The presentation insidiously conveys a great deal of information and serves as a "jumping-off point" for discussion. In spite of its lack of finesse, the production does illustrate the effectiveness of this technique in the

storage and retrieval of information, in the maintenance of cohesion of knowledge and in the condensation of knowledge. In addition, "Alice's Pharmacological Odyssey" managed to capture the attention of the audience.

6. Consultation Sheets

The idea of a Drug Information Communication Sheet originated in Mercy Hospital, Pittsburgh (12). It resulted from the need for a more positive and active role for the pharmacist in communicating drug information to the physician. Initiation of this program placed the pharmacist in the role of providing point-of-use information concerning a particular patient's drug therapy whether or not it was requested, that is, "potential information".

The communication sheet used at Mercy Hospital, is simply a sheet of paper with a line drawn down the middle. One side is used by the pharmacist for delivery of what he considers significant information or comments about the patient's drug therapy, which he follows daily. The other side is used by the physician to question further or comment on the information provided. The communications sheet is placed in each patient's chart.

In providing this type of information, the pharmacist must use judgment about its appropriateness. The information must also be positive and useful, "Sensitivity and tact are virtues that are important in the physician-pharmacist interchange. Most physicians would welcome the information obtained through the consultation program, particularly if the words 'may be' or 'could be' are used instead of declarations" (12).

The reaction of the medical staff at Mercy Hospital to the program has been favorable. However, a physician indicated that the pharmacist's education must provide him "with a new type of exposure and clinical orientation in order to meet the challenge to provide this kind of

service" (12) because, "his present education prepares him to view only a part of that whole" (12).

A similar procedure for informing physicians about potential drug interactions is being utilized at the Lions Gate Hospital in Vancouver. When the pharmacists discover a potentially significant drug interaction, they complete an interaction sheet, indicating the interactants, the effects, and the references. The information is then placed in the attending physician's mailbox. Any feedback from the physician about the clinical significance of the interaction or the usefulness of the information is encouraged.

Notifying a physician of a potential problem in his patient's drug therapy regimen has been and is and will be a professional obligation of the pharmacist. Using a communication sheet or some modification thereof may be the most convenient way of contacting the physician who is in the hospital only long enough to make rounds and then returns to his private practice. This method could not be relied upon for communicating problems of immediate urgency, since a long delay might occur before the physician became aware of the communication.

Significant progress is being made in the area of communicating drug information, particularly of the "traditional" or requested nature. Many of the methods are also being applied in supplying the "potential" information, generated from potential problems in drug usage. Whether these methods must be extended or modified in the future will not be known until a better understanding of the needs and significance of the newer trends in drug information is achieved.

D. NEWER TRENDS IN DRUG INFORMATION

The previous sections dealt with mechanisms which a pharmacist could employ to extend "traditional" and "potential" drug information. "Traditional" information is usually requested but "potential" information is usually volunteered. To be in a position to volunteer this information about a patient's drug therapy, the pharmacist must be aware of the patient's total drug picture and related therapy.

In the hospital the patient's chart is a storehouse of information about the patient's medical history, current condition and current therapy. It allows the pharmacist "to observe and comprehend the complexities of the effect of therapy on drugs and the effects of drugs on therapy" (88). However, for the purpose of following the patient's drug therapy, and thereby detecting any potential problems to communicate to appropriate health care personnel, the chart is unwieldy.

Thus, drug profiles have evolved. "The intent of the patient drug profile is to consolidate pertinent facts relating to a patient's drug therapy to allow the pharmacist to render a professional judgment regarding the effectiveness and safety of the patient's drug therapy" (89). Although the design of drug profiles varies from practitioner to practitioner, the information contained in them usually consists of: name, age, sex, weight, diagnosis, allergies, treatments and all drug orders with routes, dosage and schedule indicated (5,11,89,90,91).

By the development of such a medication profile the pharmacist is in a position to review drug therapy for potential problems as follows:

1. Drug Interactions

The literature abounds with articles on drug interactions. "A drug may potentiate or antagonize the effects of another drug by direct chemical or physical combination,

by altering gastrointestinal absorption, by influencing metabolism, transport or renal clearance, by changing the activity of a drug at its receptor site or by modifying the patient's response to the drug by a variety of means" (92). These drug interactions must be viewed in perspective. A recent epidemiological study (93) suggests that drug interactions may not be the large problem in hospitalized patients that many authors have purported. "Drugs which interact are used together -- and often with no problem. The important part is that the physician realize that there is the potential for an interaction and the possible alteration of effect. Very seldom does the situation arise where two drugs cannot be used together" (94). Nonetheless, both the physician and pharmacist must be cognizant of the possibility of interaction especially in the absence of an expected effect.

Drug-laboratory test interference

Similarly, the literature reports drug-induced modifications of laboratory test values, however, few studies are available which document the incidence of drug-diagnostic test interference.

"Drugs may alter laboratory test values through a variety of pharmacological, physical or chemical mechanisms" (95). Often the literature does not state the particular laboratory method or procedure affected by the drugs. A recent study on drug interference with laboratory test values (96) indicated that 12.8 per cent of the potential interactions yielded results corresponding to those reported in the literature. This finding implies that the problem of drug-laboratory test interference may also be overstated. Arising out of this study, is the recognition of the need for detailed studies to determine the clinical significance of such interactions.

Drug-food interactions

Foods can interact with drugs in a variety of ways to modify their effects (91). For example, the absorption of tetracycline from the gastrointestinal tract may be reduced by the concomitant ingestion of milk or other dairy products, containing calcium, which forms a non-absorbable complex with tetracycline (97,98). Another well-known drug-food interaction is the interaction between tranylcypromine and tyramine-containing foods which may result in a hypertensive crisis (99). Although these are but two examples of drug-food interactions, others are known to occur. The significance of these interactions is not always known; however, the fact that some foods can alter the effects of certain drugs should be born in mind when patients have these drugs prescribed for them.

Problems related to drug interactions appear to be publicized more than demonstrated at the present time. The significance of these problems should not be determined, however, by guesswork. It is anticipated that continuing research and more incidence evaluations will progressively develop the true picture in perspective.

2. Adverse Drug Reactions

"No matter how skillfully used, a drug that helps anyone will occasionally harm someone" (100). Moser (101) has stated that approximately forty new diseases or syndromes have developed as a result of drug therapy. In an article on drug reactions Melmon (102) indicated the importance of the problem by saying:

> "Modern therapeutic agents have contributed favorably to the physician's ability to influence the course of many diseases. Their use has also created a formidable health problem: 18 to 30 per cent of all hospitalized patients have a drug reaction, (103,104) and the duration of their hospitalization is about doubled as a consequence (64,103-105). In addition, 3 to 5 per cent of all admissions to hospitals are primarily for a drug reaction, (103,106) and 30 per

> cent of these patients have a second reaction during their hospital stay. The economic consequences are staggering: one seventh of all hospital days is devoted to the care of drug toxicity, at an estimated yearly cost of $3,000,000,000," (107).

Although the problem of adverse drug reactions is generally accepted, meaningful quantitative data is largely lacking (108). Incidence rates ranging from 0.41 to 30 per cent are reported (64,103,105,109,110). Because of the different criteria used in these studies, "today one can seldom make meaningful comparisons of the incidence of adverse reactions to different drugs or to the same drug at different dose levels or in different populations or diseases" (111).

In order to overcome the problem of adverse drug reactions, more information on the frequency and causes of adverse drug reactions and the role of influencing factors is necessary. It is believed that meaningful data can be obtained through intensive hospital monitoring (112-114, 116). Numerator data (number of patients with adverse reactions) and denominator data (number of patients exposed to drug) can be obtained through this method (109,112) but it is impossible to obtain this information from a voluntary reporting system (113). The Drug Surveillance Program in Boston (114) and one in London, Ontario (113) are collecting this type of data as part of their programs and the World Health Organization proposes the establishment of similar international programs (112).

Through the use of the methods of clinical pharmacy, a pharmacist can be a contributory participant in adverse drug reaction programs. Patient medication interviews and patient drug profiles have obvious applicability and usefulness in the collection and consolidation of pertinent data to assist a clinician in judging if a certain response of a patient could be attributable to his medications. Also, these methods provide necessary patient information to

report to a local or national adverse drug reaction program. Moreover, through the use of the various communication techniques, the pharmacist can disseminate information about adverse drug reactions.

3. Utilization Reviews

Utilization studies serve to provide information about rates and patterns of local drug utilization (117). The need for utilization reviews is based upon several factors according to Brodie (118): "a concern for public policy related to prescription drugs, the cost implications of increasing utilization, a general misuse of many drugs, the apparent irresponsible prescribing habits of many physicians, the lack of scientific knowledge of the action of many drugs in people who are ill, the ineffecient utilization of manpower in the existing pattern of drug utilization and a certain psychological dependence that society in general has on drugs."

Although utilization reports vary, "summaries showing drug utilization by specific drug or class of drugs, individual patient or all patients on a particular service and for one point in time or over a period in time" (119) can be prepared. These utilization reports are useful for cost control but their importance in promoting more effective use of drugs is foremost (120). The H.E.W. Task Force on Prescription Drugs defines utilization review as: "In any drug program, utilization review is a dynamic process aimed first at rational prescribing and the consequent improvement of the quality of health care and second at minimizing needless expenditures" (107).

Patient drug profiles are a convenient source of adequate patient and drug usage data for the preparation of utilization reviews which provide information on various aspects of drug selection, drug utilization and even drug performance. Such reviews, "depicting the local character of drug usage can provide the basis of reports to responsible

members of the medical staff or to an appropriate hospital committee (i.e., the Pharmacy and Therapeutics Committee) where they will be interpreted, evaluated and used to substantiate a recommendation to improve the situation, if the facts so indicate" (119).

4. Others

Allergies

Patients are routinely questioned to determine whether they have allergies. Suspected or known allergies to drugs are recorded on the patients' medication profiles to insure that these drugs are withheld. Sometimes these drugs may occur as constituents or combination products, and hence may be unsuspectingly administered in that form. For example, a patient with an allergy to aspirin may have propoxyphene compound (Darvon Compound Pr) which contains aspirin prescribed for him. A profile documenting the drug allergy and the medications ordered allows a pharmacist to detect potential problems at a glance. Furthermore, "hidden items in pharmaceutical bases such as alcohols in elixirs or parabens in ointment bases or injections" (88) are often allergenic and can be brought to the attention of a physician suspecting an allergy.

Contraindications to drug therapy

A multitude of diseases can alter the pharmacology of drugs. Certain pathologic states seem to predispose adverse drug reactions and certain diseases represent absolute contraindications to some drugs. For example, the use of barbiturates in a patient with a personal or familial history of acute intermittent porphyria is contraindicated (121). Care must be taken that the patient does not inadvertently receive a contraindicated drug. The patient's medication profile is useful in this respect.

Preventing duplication of drug orders

Duplication of prescription orders is a possibility

in an institution where more than one doctor can prescribe for the same patient. For example, in teaching hospitals, interns and residents may prescribe medications in addition to the attending physician. Another possibility for duplication exists in the unintentional prescribing of a combination product containing an ingredient which has already been prescribed as a single drug or vice versa.

Medication errors

Medication errors are of great concern to all hospital personnel involved in the patients' drug therapy. American and English investigators (122-124) have discovered medication error rates ranging from 13 to 18 per cent in institutions with conventional drug distribution systems. These include omitted doses, wrong doses, extra doses, unordered drugs, wrong dosage forms and wrong time (125,126) and they may result from a nursing or a pharmacy error.

Some of these medication errors can sometimes be detected by a pharmacist while maintaining medication profiles, particularly if the profile follows drug administration dose by dose. Potential errors originating from the physician's order (125) due to incorrect nomenclature, inappropriate dosage, incorrect or unspecified route of administration and illegible written orders can be recognized during the preparation of a profile and consequently brought to the attention of the physician and prevented. With the increased trend of pharmacists in institutions receiving the physicians original order and of implementation of unit dose dispensing, there is an improvement in decreasing the medication error problem (127,128). Pharmacists are continually investigating methods of identifying and of eliminating medication accidents in order to ensure patient safety.

In addition to developing the newer trends of drug information which were just described, the patient drug profile is an excellent teaching tool. Because the

initiation and maintenance of a drug profile entails abstracting pertinent patient and drug information from the chart, the student is exposed to drug therapy in the total context of the patient's condition. This enables the student to correlate pharmacological and sometimes pharmaceutical information about a drug with its therapeutic and physiological effects which are sometimes indicated in the physician's and nurse's notes and in the laboratory reports. Furthermore, the student is made aware that patients usually have more than one disease and sometimes the drug of choice for one disease is contraindicated in a concomitant disease. In such cases, the physician must weigh the benefits of the drug against its risks and often his decision may appear irrational to someone unfamiliar with the total picture.

Although drug profiles have wide application in reviewing drug therapy and in teaching, they are time-consuming to prepare and to maintain. "The data must be collected, analyzed and decisions made" (89). Smith (89) has estimated that on the basis of 100% efficiency the average pharmacist time required per patient day is 10 minutes. Thus, it becomes apparent that it is not economically feasible to review each patient's drug therapy by this mechanism.

This raises some questions: Is it necessary to maintain a drug profile on each patient? Can a system of patient priorities be established and on what basis? Do short term surgery patients such as those with tonsillectomies require monitoring of drug therapy? How effective is monitoring by pharmacists? How many significant drug therapy problems can be detected by pharmacists? Questions such as these must be answered before pharmacy and indeed hospitals accept medication profiles as a standard service procedure. In this respect one point becomes apparent. The answers to all of the above cannot and should not be attempted to be solved by one individual in one study. The many and

different variables related to drug interactions, adverse reactions, and drug utilization, for example, should be examined individually in each institution. This approach should develop clinical pharmacy as a meaningful contribution to better patient care.

III STATEMENT OF PROBLEM

To achieve the goal of "drug-use control" or in other words safe drug therapy for the patient, the task of drug monitoring and subsequently providing "potential" drug information has been widely advocated as an integral part of the pharmacist's function. "While much has been written over the recent years concerning drug interactions, the safe administration of drugs, and the need for pharmacists in hospitals to develop an effective drug monitoring program, little information has been available concerning the efficacy of drug monitoring programs, personnel requirements, time involved in screening patient orders or the expected additional expense to the pharmacy department for providing a medication profile review service on a regular basis" (7). These factors must be determined in order that a relevant clinical pharmacy approach can be designed in a hospital of any size, be it a teaching and research hospital, a community hospital or an extended care facility. The evaluation of some of these factors will be attempted in the present study through the following objectives which include:

(1) To determine the scientific validity and significance of reported penicillin-drug interactions.

(2) To determine if the reported potential penicillin-drug interactions occur in clinical practice.

(3) To determine if potential penicillin-food interactions occur in clinical practice.

(4) To comparatively evaluate the amount of pharmacist's time required for the surveillance of potential drug-drug interactions and potential drug-laboratory test interactions through a centralized and decentralized (ward) reviewing approach.

IV EXPERIMENTAL DESIGN

This research project was designed in an attempt to identify and to evaluate some of the problems facing the implementation of clincial pharmacy practice and to compare two systems of reviewing drug therapy. Since it was beyond the scope of this project to undertake the investigation of all listed drug interactions for the fulfilment of objectives 1, 2 and 3, (see p. 43) it was decided that the study of one drug would exemplify some of the problems. Penicillin G was selected as the agent to study because, on perusal of the indices, it was noted to interact with several agents, because it was considered to be a commonly used drug, and because its interactions with laboratory tests were being investigated in a similar concurrent study. In fulfilment of objective 4, it was found necessary not to restrict the study to patients on penicillin G. During this phase, penicillin G usage was low in both hospitals; thus, to acquire an adequate sample in the shortest time, patients on any type of drug therapy were followed.

The study of objectives 2, 3, and 4 was conducted in two different hospitals, A and B. Hospital A was a 1000-bed teaching-research hospital; hospital B was a 500-bed community hospital. In hospital A, medications, laboratory tests, and treatments were ordered by house-staff in addition to the attending physician whereas in hospital B usually only the attending physician wrote orders. The drug ordering system in hospital A involved a transcribed prescription being sent to the Pharmacy. No written orders for ward stock drugs, laboratory tests, or related therapy were forwarded to the Pharmacy. In hospital B, the original physicians' order sheet was sent to the Pharmacy each time an order was written. In hospital B laboratory test results were returned to the wards via the Pharmacy. In addition, the Pharmacy in hospital B received

a completed application for admission form (see Appendix VII) which contained a brief history of the newly admitted patient and orders for admission medications and laboratory tests. The patient information available to the Pharmacy in hospital B provided the opportunity for a centralized approach for the surveillance of drug therapy. In hospital A, the decentralized or ward approach was used in reviewing drug therapy.

A. LITERATURE EVALUATION

Valid and significant information sources are essential for drug surveillance programs. During the residency component, it was discovered that the evidence to validate potential drug interactions was sometimes unavailable or inadequate. "Many of the most quoted interactions are poorest in documentation. Reviews often devote as much space to one questionable case history as they do to a well conducted study. No differentiation is made between animal data and human data even when the original article pointedly denotes species differences, particularly in drug metabolism. Finally, some reviews provide no references" (129). This defined the necessity to evaluate the references documenting the listed drug interactions.

Literature, documenting the interactions between penicillin and other drugs was evaluated in this phase of the project. An exhaustive search of all of the literature on penicillin-drug interactions was not attempted since the amount of literature was considered too voluminous. Thus, the following approach was used:

(1) The potential penicillin-drug interactions stated in four indices (130, 131, 132, 133) were identified.

(2) The references listed in the indices to support the stated interactions were located.

(3) The references were evaluated with the assistance of a printed evaluation form (see Appendix VIII) and on the basis of personal examination, of interprofessional communication and of parameters set out in various guides (23,24,134).

(4) The articles were evaluated with reference only to the penicillin-drug interactions which were listed in the indices.

B. MEDICAL RECORDS SURVEY

Although the literature abounds with reports of drug interactions, there is little indication of the incidence of any of these interactions. "At present the only indicator of incidence is the number of reports in the clinical literature" (129).

To obtain some indication of the frequency of the co-prescribing and the co-administering of penicillin G with potentially interacting drugs a retrospective survey of medical records of patients, having received penicillin G, was made. The retrospective approach was utilized since no attempt was to be made to evaluate the clinical significance of any of the identified interactions and since this approach was considered more expedient.

This survey was conducted in the following manner:

(1) In hospital A, the medical records librarian was provided with a list of names of patients who had received penicillin G therapy and was asked to locate thirty files. This list of names was obtained from the pharmacy prescription files, randomly selected. In hospital B, a list of names of patients on penicillin G therapy was obtained from a survey list of patients who had received antibiotic therapy and submitted to the medical records librarian. A total of thirty files were located in hospital B also.

(2) Pertinent data from the patient's chart was recorded on a preprinted survey form (see Appendix IX).

(3) The incidence of potential penicillin G-drug interactions, as listed in the four indicies (130,131,132,133) was determined. A potential penicillin G-drug interaction was defined as the concurrent administration or the administration within 4-6 hours of the penicillin G and potential

interactant. The clinical significance of the potential interactions was not established since the main objective here was to see if the potential problems as reported in the literature do occur in practice. If they do, then mechanisms must be established to efficiently identify these before any further studies of clinical significance can be undertaken.

C. PENICILLIN G-FOOD INTERACTION STUDY

The penicillin G-food interaction is apparently accepted as common knowledge. Although acknowledgment of the interaction is made there are few references made to original research articles. Drug references such as the CPS* and pharmacology texts state that oral penicillin G should be administered no later than one-half hour before meals and no earlier than two hours after meals.

It is recognized that the absorption of oral penicillin G from the gastrointestinal tract, which is only 15 to 30 per cent of the administered dose under favorable conditions (135,137), is decreased further by the presence of food (135,136,138). Early investigators believed that food interfered with penicillin G absorption by stimulating acid secretion (139); however, it has since been postulated that the adsorption of the penicillin G onto food particles is the more likely mechanism of interference (135,136). Furthermore, because the presence of food decreases gastric emptying time it has been proposed that the ingested penicillin G reaches the duodenum in smaller concentrations and perhaps for this reason lower serum levels were obtainable and demonstrable in the trials (140). Related to the decreased gastric emptying was the suggestion that the prolonged exposure of penicillin G to the acidic gastric contents contributed to its distruction.

With this evidence that the presence of food in the stomach influences the absorption of orally administered penicillin G markedly it was decided to determine whether in the two hospitals studied, penicillin G was administered within the period one-half hour prior and two hours following meals.

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*The CPS, the Compendium of Pharmaceutical Specialties, is a compilation of monographs of prescription products published by the Canadian Pharmaceutical Association, Inc.

The survey was conducted in the following manner:

(1) A total of 60 observations of penicillin G administrations were made in the two hospitals: 27 in hospital A and 33 in hospital B. Because oral penicillin G usage was low in both hospitals during the study, patients in any service were observed.

(2) The names of the patients receiving oral penicillin G therapy were obtained from prescriptions or physicians' order sheets in the Pharmacy Departments in the respective hospitals.

(3) Nurses on the wards where these patients were located were provided with forms (see Appendix X) and were asked to record on them the exact time of penicillin G administration at mid-day and in the evening. To avoid bias in reporting the administration times, the nurses were not informed about the actual purpose of the study.

(4) Schedules of meal deliveries to the nursing stations were obtained from the dietary offices in each hospital. A few random observations of meal deliveries indicated that the deliveries were punctual, usually arriving on the ward within 5 to 10 minutes of the scheduled time.

(5) The incidence of potential penicillin G-food interactions was determined by considering the administration of penicillin G relative to the scheduled meal time rather than the actual time. It was decided to use the scheduled time of meal delivery,because the nurse has no way of predicting when a meal delivery might be delayed or early or when a patient might actually ingest his meal. A potential penicillin G-food interaction was defined as one when penicillin G was administered within the period of one-half hour

before and two hours after the scheduled meal time.

D. COMPARATIVE EVALUATION OF TIME REQUIRED FOR SURVEYING DRUG THERAPY

Two approaches of drug therapy surveillance were comparatively evaluated. The decentralized (or ward) approach was studied in hospital A and the centralized approach was studied in hospital B.

The centralized approach was possible in hospital B because the Pharmacy Department received adequate patient information. The information received by the Pharmacy Department in hospital B included:

(1) Physician's Order Sheet (original copy) which contained all drug, laboratory test, other diagnostic procedures and treatment orders.

(2) Application for Admission Form which contained patient information, diagnosis, concise medical history, drug history, new orders (drug and diagnostic procedures), drugs administered in Emergency if the patient was admitted through there, and special instructions.

(3) Laboratory Test Results.

In hospital A (decentralized approach) only a transcribed prescription for ordered drugs was received in the Pharmacy Department, often lacking pertinent information such as drug strength. All of the information necessary for the surveillance of drug therapy was abstracted from the patients' charts.

Arrangements were made with the pharmacy departments and nursing stations to minimize interference with the functions of their staffs.

The study was conducted in the following manner:

(1) In each hospital, patients were randomly selected from the previous day's admission sheets until a total of ten patients in each of three services (pediatrics, medicine and surgery) were obtained. Therefore, a total of thirty patients were

followed in each hospital.

(2) Each patient's drug therapy was followed for five days or until discharged, whichever occurred first.

(3) In hospital A (decentralized approach) surveillance of the patients' drug therapies was conducted on the wards by utilizing the patients' charts. In hospital B (centralized approach) surveillance of drug therapy was conducted in the Pharmacy Department by utilizing the information sent to it.

(4) The amount of time required to follow the patients' drug therapy was clocked with a stopwatch. Interference time which included discussions unrelated to the study and travel time was also noted and recorded separately.

(5) The amount of time required to review drug therapy was categorized as follows:

   a) Profile Initiation Time: This was defined as the amount of time required to abstract the essential patient information from the patient's chart or an application for admission form and to transfer it to the profile form (see Appendix XI) when the patient was admitted.

   b) Profile Maintenance Time for Drug-Drug Interactions: This was defined as the amount of time required to identify newly ordered and discontinued drugs, to update the profile and to identify from the "Drug Interaction Index" (130) any interactions between the ordered drugs. Although drug interactions may occur between two or more drugs, for the purposes of this study, interactions between only two drugs were considered. Thus, groups of two different drugs made a combination which was investigated for a potential interaction. The figures in Table IV (see page 68) represent the

number of combinations investigated and not the number of potential drug-drug interactions. The potential interaction and its effect were recorded on the profile form.

The time required to review one drug-drug interaction was determined in the following way:

The total amount of time required to review drug therapy for drug interactions for the period that the patient was followed was divided by number of drug-drug combinations that were possible in the patients drug therapy regimen. The number of combinations was determined by the mathematical formula $n^{C}2$ where "n" was the total number of new drugs ordered for that patient. It must be noted that this figure did not represent the number of potential drug-drug interactions as reported in the indices.

Patients, receiving one drug or less during the period they were followed, were eliminated from this portion of the study.

c) Profile Maintenance Time for Drug-Laboratory Test Interactions: This was defined as the amount of time required to identify and record laboratory tests ordered, to record laboratory test results, to determine from "Drug-Induced Modifications of Laboratory Test Values" (95) whether any of the patient's drug therapy interfered with the laboratory test values and to record the interactions and their effects on the profile form. Only interactions between one drug and one laboratory test at a time were considered. Because it was usually impossible to determine whether the test was performed before or after a

drug had been ordered, drugs ordered on the same day as the laboratory test, in addition to those ordered and used before the laboratory test was ordered were investigated for potential interactions. This arbitrary approach seemed justifiable since it would influence both surveillance systems being comparatively evaluated in the same way.

Included in the profile maintenance time for drug-laboratory test interactions, was the time for reviewing and recording culture and sensitivity reports.

The time required to review one drug-laboratory test interaction was calculated as follows:

Total amount of time required to review drugs and laboratory tests, ordered during period of time which the patient was followed was divided by the number of combinations of drug-laboratory tests that were possible. The number of drug-laboratory test combinations were counted. It must be noted that this figure did not represent the number of potential interactions. Only those patients receiving one or more drugs and having one or more laboratory tests were included in the calculations in this portion of the study.

V. RESULTS AND DISCUSSION

Literature Evaluation

In reviewing the literature cited in the indices in support of the listed penicillin-drug interactions both valid and invalid references were found. In general it was found that the indices were inadequately referenced to make a reasonable judgment on the soundness of each reported interaction. As Hartshorn points out (129), the reviews and charts on drug interactions often make generalizations and indiscriminately mix animal and human data. Sometimes there are no references provided and sometimes other reviews or indices are listed as references. Although some well-designed studies were quoted to substantiate the interactions, these were infrequent. Some examples of the types of shortcomings encountered in the evaluation of the reported interactions are presented as follows:

(1) Incorrect references were listed for some interactions. In the "Drug Interaction Manual" (133) an interaction between penicillin and amisometradine was stated. Upon examining the review article which was given as the reference, no mention of the interaction could be discovered.

(2) The absence of any references to support a stated interaction occurred. Interactions between penicillin and antacids and between penicillin and acid media were claimed in the "Handbook of Drug Interactions" (131). However, no original research was quoted to support either interaction or to indicate the clinical significance of either one.

(3) Frequently other indices or review articles were named as references; that is, no reference was made to original research. The "Drug Interaction Index" (130) used review articles as four out of the five references it listed in support of the penicillin-drug interactions.

(4) Some of the quoted sources were not available in the local biomedical library system. Articles in the periodical,

"Hospital Formulary Management" could not be obtained for evaluation because the local library did not subscribe to this periodical.

(5) Many of the research papers which were cited, were "in vitro" or animal studies. It is generally agreed that "in vivo" evaluation need not coincide with "in vitro" results. Furthermore, interspecies differences are large and the speed and pathway of metabolism of a drug in man may be very different from that which has been determined in the laboratory animals. The original research, listed in support of the claim that the effect of penicillin is enhanced by streptomycin (131), was "in vitro" and animal data (141,142) and no reference was made to any clinical or human evidence. During the literature search some clinical evidence was discovered for this synergistic interaction. Synergism had been demonstrated when combined penicillin and streptomycin therapy was used in the treatment of bacterial endocarditis, caused by some strains of some species of enterococci (143,144). This situation illustrated the fact that inadequate literature searches by the compilers of indices can miss meaningful evidence, in addition to the problem that "in vitro" and animal data are used as supporting references.

(6) Conflicting reports occurred in the literature. Three indices (130-132) stated that erythromycin antagonized the bactericidal effect of penicillin. On examining the references (145-147) it was found that this effect was not always demonstrated; at times a synergism was observed. It was found that different test inocula, different organisms and different concentrations of these antibiotics were used and that these variations were likely responsible for the conflicting results. Furthermore, the time relationship is important in observing antagonism: the interfering agent must act on the bacteria either simultaneously or before the bactericidal drug not after (148). This means that in

the clinical situation where there is multiple-dose treatment, it is difficult to observe antagonism because of the ever-changing blood and tissue levels of the two drugs. Some authorities (149,150) believe that antagonism between antibiotics is of little clinical significance. Thus, in a situation such as the forementioned example, where results were equivocal, it was misleading to list only one effect of the drug interaction.

(7) Generalizations about a group of drugs were made on the basis of the results obtained from the study of one drug. For example, oral chymotrypsin was reported to potentiate penicillin activity by enhancing absorption. Examination of the reference (151) revealed that phenethicillin was the only penicillin investigated. However, phenethicillin differs in acid stability and extent of absorption from most of the other penicillins (152). Therefore, although the research for phenethicillin absorption was well-designed, it was considered not justifiable to extrapolate the findings for phenethicillin to all other penicillins.

(8) Studies without any controls were encountered. A clinical trial by Sabath (153) was conducted to demonstrate synergism between the penicillinase-resistant penicillins (acting as beta-lactamase inhibitors) and benzylpenicillin. Patients with chronic bacteriuria were treated with the combination but no controls of any nature were used.

(9) Some well-designed studies were cited as references; however, the clinical significance of the interactions was not indicated in the indices. Kunin's research (154) on drugs which displace penicillins from protein-bound sites was found to be a well-designed and statistically analyzed study. Kunin was able to demonstrate displacement of the penicillin analogues by certain drugs; however, he cautioned that this was likely of limited clinical significance because of the high doses of these agents which were required

for the effect. Since the indices do not indicate the clinical significance of the listed drug interactions, this exemplifies the need to examine the original research to determine this.

Similar shortcomings and limitations in the literature and in the indices on penicillin-laboratory test interference were encountered by Kane (155) in a related study.

The problems, identified in this phase of the project and by Kane (155) demonstrate the fact that the penicillin-drug interactions, reported in the indices, are not well-documented. It is probably a safe assumption to suggest that the majority of drug interactions are not well-documented. Moreover, these problems illustrate the difficulties that all pharmacists and health personnel must face in attempting to obtain valid information.

Although this project illustrated only some of the limitations of the indices and the literature, pharmacists and other health professionals must be made aware that there are many shortcomings. Reported drug interactions should not be interpreted as valid without first examining and evaluating the references.

The indices have served the function of identifying and tabulating drug interactions. However, in order for the pharmacist to play a more meaningful role in the surveillance of drug interactions the following objectives must be met:

1. There is a need for more and, in some cases, improved scientific research on drug interactions. The research must be of a nature, relevant to the clinical situation and it appears that "Trial in man is the only way of establishing drug interaction in man" (156). Questions such as "why there is a potential interaction, what the chances are for the interaction to occur, how important it is to the patient's health and what can or should be

done about it" (129) must be answered about each reported drug interaction.

(2) There is a need for a system of primary and secondary references to expedite the identification of valid drug interactions and the dissemination of information about them. The primary reference which could be considered a guide, would consist of drug interactions, validated by research, and presented in a manner facilitating easy retrieval. Each interaction would be adequately documented.

The secondary reference system would support the primary reference. It would consist of valid and evaluated available data, interpreted and assessed in terms of clinical significance by qualified individuals. This type of comprehensive and authoriative information source is currently being developed by the American Pharmaceutical Association*.

(3) The pharmacist's training and education must be oriented so that he can make a meaningful contribution in the area of drug interactions. He must be able to identify potential drug interactions (through the use of primary references); he must be able to ascertain which drug interactions might be of clinical significance (through the use of secondary references); and he must be able to communicate relevant information about drug interactions in perspective to the various health professionals.

Medical Records Survey

From the retrospective medical records survey, it was apparent that potential penicillin G-drug interactions, as listed in the indices, do occur (see Table I). In 38 out of 60 medical records surveyed in the two hospitals, 49 potential penicillin G-drug interactions were identified. The incidence of these penicillin G-drug interactions was quite similar in both hospital A and hospital B; however,

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* "Evaluations of Drug Interactions", a pilot project, 1971, American Pharmaceutical Association, 2215 Constitution Avenue, N.W., Washington, D.C. 20037.

TABLE I

INCIDENCE OF POTENTIAL PENICILLIN G[1] - DRUG INTERACTIONS[2] AS DETERMINED FROM A MEDICAL RECORDS SURVEY

	Hospital A	Hospital B	Total
Number of medical records reviewed	30	30	60
Number of patients with potential interactions	17	21	38
Number of potential interactions	21	28	49
Average number of interactions per patient	0.70	0.93	0.82

[1] All penicillin G salts used orally and parenterally were considered.

[2] A potential interaction was defined as one listed in the drug interaction indices. No attempt was made to determine if it occurred clinically.

the nature of the interactions differed in the two hospitals. In hospital B, 21 out of the 28 interactions had the potential of increasing the effect of penicillin G whereas in hospital A, only 8 out of 21 interactions did the same. Most of the interactions with the potential of increasing the penicillin G effect occurred between aspirin or aspirin products and penicillin G.

It was not the object of this survey to determine whether any of the identified penicillin G-drug interactions were clinically significant. Likely, few if any, of the noted interactions modified the patient's response to his therapy.

In a related study, Kane (155) found that laboratory tests were ordered for patients on penicillin G therapy whose results might be modified by the penicillin G. Kane observed 28 potential penicillin G-laboratory test interactions in 12 out of 35 medical records.

Penicillin G-Food Interaction Study

In the study on penicillin G-food interactions, it was found that approximately 70 per cent (43 out of 60) of the observed administrations of penicillin G were during a period when food ingestion might have interfered with the absorption of the penicillin G (see Table II). In hospital A 20 out of 27 administrations were within the period of one-half hour before meals and two hours after meals and in hospital B, 23 out of 33 administrations were during this period.

No attempt was made to determine if the interference resulted in a clinically significant decrease of penicillin G activity, since the evidence of potential problems was of major interest in the present sutdy. It was noted, however, that all dosages of penicillin G were at least as large as those recommended in CPS* and most were larger.

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*CPS is the Compendium of Pharmaceutical Specialties, a compilation of monographs of prescription products published by the Canadian Pharmaceutical Association, Inc.

TABLE II

INCIDENCE OF POTENTIAL PENICILLIN G - FOOD INTERACTIONS[1] OBSERVED IN TWO HOSPITALS

	Hospital A	Hospital B	Total
Number of observations[2]	27	33	60
Number of potential interactions[1]	20	23	43

1. A potential interaction between penicillin G and food was defined as one occurring upon the administration of oral penicillin within one-half hour prior to scheduled meal-time or within two hours following scheduled meal time.

2. Observations were defined as the total number of observations of administered doses of oral penicillin G.

Although the Pharmacy Department in hospital B labelled all of the oral penicillin G which it dispensed with instructions to administer it on an empty stomach, this did not ensure proper administration.

Since there is evidence (135,136,138) that the presence of food influences the absorption of orally administered penicillin G, several steps can be taken to help overcome the problem of co-administering the penicillin G with food.

(1) Phenoxymethyl penicillin (penicillin V) can be suggested as an alternative for penicillin G. Penicillin V is better absorbed from the gastrointestinal tract than is penicillin G due to its acid stability and its solubility in the alkaline medium of the duodenum (157). Serum levels three to four times greater than those obtainable with penicillin G have been demonstrated (158) however, only 35-40% of the administered dose is absorbed. Total absorption is not influenced by timing of the dose in relation to meals although peak serum concentrations occur earlier and are higher in the fasting state. There is also some evidence that the presence of food enhances the absorption of penicillin V (159).

In suggesting penicillin V as an alternative for oral penicillin G, it should be kept in mind that it is more expensive than penicillin G.

(2) In-service education programs could be established to give the nursing personnel an understanding about the importance of administering penicillin G at least one-half hour before meals or two hours following meals. If given in this manner, maximal absorption of the penicillin G is achieved. The Medical Letter (160) points out that "the recommended doses of penicillin G are high enough to compensate for acid degradation; moreover, if the drug is taken two hours before or three hours after a meal -- that is, on an empty stomach when gastric acidity is lowest -- acid

degradation is limited." With this understanding, likely the nursing personnel would make more conscious efforts to administer oral penicillin G correctly.

(3) Alternatively, the pharmacy department, the nursing personnel and the dietary department could attempt to arrange (for those drugs to be administered on an empty stomach) a more feasible drug administration schedule relative to meal times. For example, the q6h schedule, almost universally denotes that a drug is to be administered at 600, 1200, 1800 and 2400 hours. This means that at least two doses of the drug are administered at meal time or very close to it. To avoid this, perhaps a schedule of 400, 1000, 1600 and 2200 hours might be preferable. However, each nursing station would probably have to establish its own schedule, depending on food arrival time, with the assistance of the dietary and pharmacy departments.

Comparative Evaluation of Time Required for Surveying Drug Therapy

(a) Profile Initiation Time

The amount of time required to initiate drug profiles for each patient (see Table III) in three different services in hospital A (decentralized approach) was significantly greater than in the same three services in hospital B (centralized approach). Approximately a 2-fold time difference was observed between the two hospitals for each of the services. The "t"-test was used to determine the statistical significance of the data and it was found that all of the differences were highly significant, i.e., for Pediatrics "t" was 4.5; for Medicine "t" was 3.0; for Surgery "t" was 6.4; and for all services combined "t" was 5.6.

Interruption time and travel time were excluded from the profile initiation time.

TABLE III

AMOUNT OF TIME REQUIRED TO INITIATE[1] DRUG PROFILES IN DIFFERENT SERVICES OF TWO HOSPITALS

Initiation Time Required per patient in each service[2]	Hospital A (Decentralized Approach)	Hospital B (Centralized Approach)
Pediatrics	238.8 sec. (± 78.7)[3]	108.4 sec. (± 38.1)
Medicine	276.6 sec. (±161.0)	109.7 sec. (± 38.2)
Surgery	176.6 sec. (± 18.5)	108.4 sec. (± 26.1)
Mean	230.7 sec. (±111.9)	108.8 sec. (± 34.6)

1. Initiate - This function was defined as the selection and transfer to the drug profile form of appropriate patient data from the patient's chart and/or admission form.

2. Time required per patient in each service represents the mean time required to initiate drug profiles for each of 10 patients in that service.

3. Standard Deviation.

The increased time requirement in the decentralized system (hospital A) arose primarily from the need to search throughout the patient's chart to collect pertinent patient data. Furthermore, in hospital A, the patient's admission history was almost invariably more lengthy and detailed than in hospital B. An application for admission form used in hospital B, usually contained adequate and concise patient information. In addition, this form contained drug and diagnostic orders so that profiles could be initiated from a completed form. Only on occasion was it necessary to consult the patient's chart for necessary data. Frequently, (about 50% of the time) medication histories were unavailable from either the application form or the patient's chart in hospital B. In hospital A, a medication history was present in 95% of the charts studied. Neither hospital had adequate medication histories.

Although the amount of time saved in initiating profiles by the centralized approach was highly significant, there is the disadvantage of the pharmacist not being on the ward to answer questions and to handle pharmacy-related problems. However the time saved by the centralized approach could probably be more effectively used to deal with specific problems by a pharmacist making a scheduled visit to the wards. At this visit or round, the pharmacist could more efficiently communicate potential problems identified through centralized screening. The function of centralized screening could be performed by non-professional assistants.

Non-professional assistants could initiate profiles from adequately designed admission forms which had been evaluated by pharmacists and physicians.

(b) Profile Maintenance for Drug-Drug Interactions

The results in Table IV represent three factors -- a comparison of the time required by the two approaches to screen drug combinations which might be potentially interacting; a comparison of the average number of drug

TABLE IV

AMOUNT OF TIME REQUIRED TO REVIEW[1] DRUG-DRUG COMBINATIONS[2] FOR POTENTIAL INTERACTIONS IN THREE SERVICES OF TWO HOSPITALS

SERVICE[3]	HOSPITAL A (Decentralized Approach)	HOSPITAL B (Centralized Approach)
PEDIATRICS		
Time for each combination[4]	38.4 sec. (± 12.3)[7]	16.9 sec. (± 9.0)
Number of combinations per patient for period followed[5]	3.5	7.9
Time per patient day for reviewing for interactions[6]	53.2 sec. (± 20.9)	32.0 sec. (±10.5)
MEDICINE		
Time for each combination[4]	17.4 sec. (± 10.3)	9.9 sec. (± 5.0)
Number of combinations per patient for period followed[5]	19.1	32.2
Time per patient day for reviewing for interactions[6]	77.0 sec. (± 43.7)	54.0 sec. (±31.0)
SURGERY		
Time for each combination[4]	23.9 sec. (± 10.2)	7.8 sec. (± 4.5)
Number of combinations per patient for period followed[5]	11.1	31.5

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TABLE IV Continued

Time per patient day for reviewing for interactions[6]	57.8 sec. (± 17.7)	45.5 sec. (±23.6)
MEAN[8]		
Time for each combination[4]	25.1 sec. (± 13.2)	11.5 sec. (± 7.7)
Number of combinations per patient for period followed[5]	11.2	23.9
Time per patient day for reviewing for interactions	62.7 sec. (± 31.0)	44.3 sec. (±25.3)

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1. Included updating drug orders on profile and identifying and recording potential interactions and their effects.

2. Defined as a combination of two different drugs.

3. Figures in table represent the means of the results of eligible patients from a total of 10 followed in each service.

4. Total time spent in reviewing (observed) divided by total number of drug combinations.

5. Determined by formula, $_nC_2$, where n was number of new drug orders. Represents number of drug-drug combinations and not the number of potential interactions.

6. Total time spent in reviewing (observed) divided by number of days patient was followed.

7. Standard deviation.

8. Figures in this portion of table represent means of results of the total number of patients followed in each hospital.

combinations, that is, combinations of two drug orders, per patient in hospital A and B; and a comparison of the amount of time required per patient day which is an indirect result of the first two factors.

In each service there was about a two to three-fold greater time requirement in the decentralized system (hospital A) than in the centralized system (hospital B) to review drug therapy for potential interactions. The time difference between the two systems was shown to be statistically significant for each of the services through use of the "t"-test. In fact, the mean time required for each combination in hospital A was highly significantly greater ("t" was 4.4) than that in hospital B.

Probably the most important factor contributing to the time difference was the need to search through the patient's chart for new drug orders in the decentralized system. Even when no drugs were ordered, time was spent in determining this; whereas, in the centralized system if the physician's order was not sent to the pharmacy, it was assumed that no new drug orders were written. More noise, activity and distractions were encountered in the decentralized system and these could have reduced the pharmacist's efficiency. Thus, from the time-efficiency point of view, this data would appear to support a centralized versus a decentralized approach for reviewing drug therapy.

The number of drug-drug combinations which were investigated for potential drug interactions was consistently greater in each of the services in hospital B than in hospital A.

The total time required per patient day to review drug-drug combinations also appeared to be greater in each service in the decentralized approach (hospital A) than in the centralized approach (hospital B). The difference between the two systems becomes more impressive when one considers the fact that the number of drug-drug combinations

per patient was greater in hospital B (centralized approach) than in hospital A. It should be noted that the total time per patient day to review drug combinations was not the product of the time per combination and of the number of combinations per patient, as would seem logical, because the number of days for which each patient was followed varied. Rather this value was determined by dividing the total amount of time which was required to review a patient's drug therapy for the period he was followed by the number of days the patient was followed.

Although this comparative evaluation represents only the amount of time required for the identification of potential drug-drug interactions and does not include the amount of time required to establish the clinical significance of the potential interaction and to communicate this information, it might serve as a comparative guide for a pharmacist wishing to establish a drug surveillance system. This would appear to be a valid comparison since the follow through and/or communication by the pharmacist would take the same amount of time in both the centralized and decentralized systems.

Much of the pharmacist's time utilized in centralized screening could be saved through the use of non-professional assistants. These personnel could note and bring to the attention of a pharmacist the potential interactions listed in indices. The pharmacist could then concentrate his time on following up the potential drug interactions which he felt might be significant. This approach demonstrates another way in which the technical aspects of drug surveillance could be realized without creating a significant demand on the time of a professional.

(c) Profile Maintenance Time for Drug-Laboratory Test Interactions

The amount of time that was required to survey drugs and laboratory tests, ordered concurrently, for potential interactions or interference is represented in Table V.

TABLE V

AMOUNT OF TIME REQUIRED TO REVIEW[1] DRUG-LABORATORY TEST COMBINATIONS[2] FOR POTENTIAL INTERACTIONS IN THREE SERVICES OF TWO HOSPITALS

SERVICE[3]	HOSPITAL A (Decentralized Approach)	HOSPITAL B (Centralized Approach)
PEDIATRICS		
Time per drug-laboratory test combination[4]	16.9 sec. (± 6.0)[7]	14.0 sec. (± 8.2)
Number of combinations per patient for period followed[5]	14.4	23.7
Time per patient day for reviewing for interactions[6]	73.2 sec. (±39.2)	84.0 sec. (±37.5)
MEDICINE		
Time per drug-laboratory test combination[4]	13.7 sec. (± 7.3)	10.8 sec. (± 4.4)
Number of combinations per patient for period followed[5]	57.6	45.1
Time per patient day for reviewing for interactions[6]	161.6 sec. (±76.5)	100.8 sec. (±24.0)
SURGERY		
Time per drug-laboratory test combination[4]	18.6 sec. (± 7.5)	10.5 sec. (± 8.4)

Continued...Pg. 73

Table V Continued.

Number of combinations per patient for period followed[5]	21.3	29.8
Time per patient day for reviewing for interactions[6]	93.8 sec. (±51.4)	60.0 sec. (±37.0)
MEAN[8]		
Time per drug-laboratory test combination[4]	16.5 sec. (± 7.0)	11.8 sec. (± 7.1)
Number of combinations per patient for period followed[5]	31.1	32.9
Time per patient day for reviewing for interactions[6]	108.9 sec. (±68.5)	82.3 sec. (±37.3)

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1. Included updating laboratory test orders and results on profile, following culture and sensitivity reports, identifying and recording potential interactions and their effects.

2. Defined as a combination of one drug and one laboratory test ordered for the same period of time.

3. Figures in table represent the means of the results of eligible patients from a total of 10, followed in each service.

4. Total time spent in reviewing (observed) divided by total number of drug-laboratory test combinations.

5. Determined by counting number of combinations of one drug and one laboratory test. Does not represent number of potential interactions.

6. Total time spent in reviewing (observed) divided by number of days patient was followed.

7. Standard deviation.

8. Figures in this portion of table represent means of results of the total number of patients followed in each hospital.

Although this aspect would be ordinarily reviewed simultaneously with drug-drug interactions, it was subdivided in this study since procedures for laboratory test orders and results were somewhat more complicated than for drugs. Individual hospital laboratory procedures, time interval between order and results, nature of recording results (i.e., with or without normal values), and method of inserting results in chart (for example, all hematological results on one sheet or at random) were some of the variable factors which influenced the time requirement for reviewing drug-laboratory test combinations for interactions.

The amount of time required to screen drug-laboratory test combinations for potential interactions per patient was greater in the decentralized system than in the centralized one for each of the services surveyed. The mean difference between the two systems (16.5 seconds by the decentralized approach versus 11.8 seconds by the centralized approach) was statistically significant as determined by the "t"-test ("t" was 2.4).

A computerized print-out of laboratory test results in hospital A was probably the most important factor in making the time requirement difference between the two approaches less marked. Although it was still necessary to locate the laboratory data in the patient's chart in the decentralized approach, once located the results were presented in an orderly fashion. That is, all of the results and normal values of laboratory tests, ordered on one day, were reported on one sheet. Also a cumulated report of all test results replaced the daily report once a week. On the other hand, in hospital B the laboratory test results were returned on the individual requisitions as they were completed, and often normal values were not included on the reports which necessitated reference to a table.

In the two hospitals the mean numbers of drug-laboratory test combinations per patient were approximately

equal. Although more drugs per patient were ordered in hospital B (see Table IV), more laboratory tests per patient were ordered in hospital A.

The mean time required per patient day for reviewing drug-laboratory test combinations was greater in hospital A (decentralized approach) than in hospital B (centralized approach) in spite of the fact that the number of drug-laboratory test combinations were approximately the same in both hospitals. It must be noted that the time required per patient day for reviewing drug-laboratory test combinations was not a product of the time required per combination and of the number of combinations since patients were not all followed for the same length of time.

This value was obtained by dividing the total amount of time required to review drug-laboratory test combinations by the number of days which the patient was followed.

A difference in the amount of combined time required to review drug-drug and drug-laboratory test combinations for potential interactions was observed amongst the three services included in the study (see Table VI). In both hospitals the mean combined time per combination was greater in pediatrics than in medicine and surgery.

Although fewer drugs and laboratory tests were ordered in pediatrics, it appeared that the efficiency in reviewing these was less than in the other services. Some of the explanations for this might be that the directions for administration of drugs to pediatrics were more explicit than in the other services. Thus, more time was spent in transferring this information onto the profile. Another factor, contributing to the increased mean combined time requirement in pediatrics, might be the fact that the majority of pediatric patients were receiving antibiotics. This meant that more culture and sensitivity studies were reviewed and recorded.

TABLE VI

COMPARATIVE AMOUNT OF TIME REQUIRED TO REVIEW[1] DRUG-DRUG COMBINATIONS[2] AND DRUG-LABORATORY TEST COMBINATIONS[3] IN DIFFERENT HOSPITAL SERVICES

	Hospital A (Decentralized Approach)	Hospital B (Centralized Approach
Mean time per combination[4]		
Pediatrics	27.6 sec.	15.4 sec.
Medicine	15.5 sec.	10.3 sec.
Surgery	21.2 sec.	9.1 sec.
Total time per patient day[5]		
Pediatrics	126.4 sec.	116.0 sec.
Medicine	238.6 sec.	154.8 sec.
Surgery	151.6 sec.	105.5 sec.

---

1. Included updating drug and laboratory test orders and results on profile, following culture and sensitivity data, identifying and recording potential drug-drug and drug-laboratory test interactions and their effects.

2. Defined as a combination of two different drugs.

3. Defined as a combination of one drug and one laboratory test, ordered for the same period of time.

4. The mean of time per drug-drug combination from Table IV and of time per drug-laboratory test combination from Table V to review these.

5. The total of time per patient day to review drug-drug combinations and of time per patient day to review drug-laboratory test combinations.

The total time per day to review drug therapy was greater in medicine than in pediatrics and in surgery in both hospitals (see Table VI). Medicine required the greatest amount of time because this service had the most drugs and laboratory tests ordered per patient (see Tables IV and V). Pediatrics required the least time per patient day because although the mean combined time required per combination was highest in this service, pediatrics had the fewest number of drugs and laboratory tests ordered per patient.

Further verification of these trends from the point of view of time efficiency would be interesting and might provide meaningful data for estimating personnel requirements in hospital pharmacies depending on the predominant service in that hospital.

It should be noted that the time requirement in the decentralized approach did not include an interruption factor and travelling time between the pharmacy department and the wards. It was found that approximately a 15% time adjustment should be added in the decentralized approach to account for these. This figure corresponds fairly closely with the 17% adjustment value determined by Slining et al (7). Furthermore, the time required to locate charts on the nursing unit or those absent from the nursing unit was not considered in the reviewing time nor the interruption-travelling time. This would increase the time requirement in the decentralized approach somewhat. All of these factors detract from the decentralized approach with respect to time efficiency.

Although this comparative evaluation represents only the time required for the identification of potential interaction problems and not the identification of other problems nor the follow-through and communication of information about identified interaction problems, it might serve as a comparative guide. A pharmacist, wishing to establish a

drug reviewing system, could refer to this data. Excluding the amount of time required to initiate profiles and not considering experimental error and variation from hospital to hospital, the amount of time required to review the drug therapy of 100 patients for potential interactions would be about 4.5 hours per day, using the decentralized approach, as compared to 3.3 hours, using the centralized approach. (These figures do not allow for interruption and travelling time.) These figures represent:

(1) the amount of time saved in the centralized approach versus the decentralized approach

(2) The amount of time required for drug surveillance of interactions which could be done by non-professional assistants under a pharmacist's supervision. This type of surveillance function is largely technical in nature and could be efficiently programmed for electronic data processing, once it became economically feasible. Until such time, non-professional assistants could identify the problems and free the pharmacist to concentrate on the significance of the identified potential problems and to communicate more effectively relevant information to the appropriate health care personnel.

One might speculate that the advantage of a decentralized surveillance system would be the presence of a pharmacist to answer spontaneous questions. However, it is proposed that a pharmacist would make rounds to further investigate those problems identified centrally and to communicate information about them. During these rounds any other questions could be handled by the pharmacist. In addition, routine pharmacy rounds could be scheduled to satisfy the information needs on the nursing stations.

VI SUMMARY AND CONCLUSIONS

There appears to be a definite need for increasing the availability of drug information to the health professionals in promoting effective and safe drug therapy. This need does not so much reflect the volume of drug information required, as a meaningful, accurate and concise evaluation of the information already available.

This objective is a primary goal of Clinical Pharmacy. It has been demonstrated, however, that pharmacy has several phases to develop before it can make a meaningful contribution in this respect. Some of these phases, as reflected in the present work, include:

(1) more clinical research to clarify the significance of currently reported adverse drug reactions and drug interactions
(2) a centralized method of evaluating and disseminating the information generated from such research
(3) an efficient surveillance program within each hospital to identify the incidence and daily occurrence of potential drug-related problems
(4) an effective use of non-professional assistants to aid in the technical aspects of such programs.

The present study has indicated that with respect to surveillance for potential drug interactions a primary index such as "Drug Interaction Index" (130) or "Handbook of Drug Interactions" (131) or a formulary may best be used for initial screening. A secondary reference index such as that being developed by the American Pharmaceutical Association would be most valuable to further evaluate the clinical significance of potential problems.

It was shown by this study that penicillin G-drug interactions and penicillin G-food interactions, as reported in the literature did occur in the two hospitals surveyed and by a related study (155) that penicillin-laboratory test interactions, as reported in the literature, did occur in

practice. This suggests that there is a need for a surveillance program on drug usage.

Two approaches (centralized and decentralized) were comparatively evaluated with respect to screening for drug-related problems, specifically for potential drug-drug interactions and drug-laboratory test interactions. It was found that in terms of time efficiency, the centralized approach, conducted in the pharmacy department, was significantly more efficient than the decentralized approach, conducted on the nursing stations and using patient's charts. Profile initiation time was only about one-half as great in the centralized approach. Profile maintenance time, including the time for identifying potential interactions, was significantly less in the centralized system also. The time saved by utilizing a centralized system of surveillance could be more beneficially used by a pharmacist to follow through, to evaluate, and to communicate relevant information about the identified problem.

The use of non-professional assistants to perform the function of identifying potential drug interaction problems in the patients' therapy, from a validated reference source would further increase the saving of the pharmacist's time. In the future, the computer will likely perform this technical function.

VII RECOMMENDATIONS

"The feasibility of the pharmacist functioning effectively in this capacity (drug-related patient care) has now been sufficiently demonstrated so that the question is no longer one of the appropriateness of this role, but rather how best it can be developed" (13).

1. There is a need for a more patient-oriented education for the pharmacist. The training and education should be so designed "to create a coordinated learning process whereby theory, fact, skill and clinical application will be integrated, for and by the student, within and between disciplines and implemented in practice at the patient level" (32). The pharmacist must be prepared to provide selective, reliable and problem-oriented drug information when and where it is needed in patient care.

2. There is a need for an integrated approach in educating the health professionals so that each discipline has an understanding of the other's background and capabilities. This would foster teamwork, mutual respect and improved communications.

3. There is a need for the development of comprehensive, regional drug information centers which could extend support into those areas where limited availability of resources results in a more pressing need for practical pharmacotherapeutic information. In Canada, a few such centers affiliated with the major medical and pharmacy schools and utilizing modern communications technology could serve the needs of the whole country.

4. It is imperative that the pharmacist present only valid and clinically significant information to the health professionals. The masses of literature about drugs must be evaluated before communicated. Most of the reported drug interactions must be validated -- a project with which the American Pharmaceutical Association is currently engaged.

5. There is a need for an international exchange of drug information, coordinated by some body such as the World Health Organization. W.H.O. has already taken a step in this direction by establishing an international drug monitoring program for adverse drug reactions (161).

6. Greater utilization of the computer must be made in pharmacies. "Properly appreciated, tamed and utilized, the computer will undoubtedly improve pharmacy service and contribute to the optimum in patient care" (162). The computer is currently being employed by pharmacies to perform a variety of functions (163). It's use in drug utilization and drug surveillance and screening drug therapy for interactions is now recognized and is being developed. Although the computer frees the pharmacist from many technical tasks, a pharmacist's professional judgment is required to determine the significance of the identified problems.

APPENDIX I

PHARMACEUTICAL PRODUCT INFORMATION FILE

NOMENCLATURE:

1. Non-Proprietary Name

2. Proprietary Name(s) and Manufacturer(s)

3. Foreign Proprietary Name(s), Country, & Manufacturer(s)

CLASSIFICATION

4. Pharmacological-Therapeutic Classification

5. A.S.H.P. Formulary Number

6. Legal Classification: Narcotic____, Schedule G ____, Prescription Drug ____, Non-Prescription Drug ____.

7. Status: Approved ____ Investigational ____

CHEMISTRY

8. Chemical Classification

9. Chemical Name

10. Structural Formula:

11. Molecular Weight

12. Physical Properties
    Solubility in Water______, Alcohol_____, Others __________
    pH______________

eference
Number

13. Chemical Properties

14. Physical and/or Chemical Incompatibilities

15. Attach official assay methods

PHARMACOLOGICAL ACTION

16. Mechanism of Action

17. Site(s) of Action

18. Onset of Action

19. Duration of Action

20. Site(s) of Absorption

Transport and Distribution

21. Does this drug pass the CNS barrier?: Yes_____ No _____

22. If "Yes" in (21) to what extent?:_____% of dose given.

23. Does the drug pass the blood-brain barrier? Yes___ No____

24. If "Yes" in (23) to what extent?: _____% of dose given.

25. Does the drug pass the placental barrier? Yes____ No______

26. If "Yes" in (25) to what extent?: _______% of dose given.

27. Site(s) of detoxification

28. List all metabolites and catabolites.

29. Site(s) of excretion

30. Half-life of the drug

31. List the excretion products.

INDICATIONS FOR THERAPEUTIC USE

32. List indications for use.

WARNINGS AND UNTOWARD EFFECTS

33. List all side effects, allergies and hypersensitivities.

Reference Number

CONTRAINDICATIONS

34. List disease and patient condition-related contraindications.

35. List drug and food-related contraindications

INTERACTIONS

36. List any prescribed drugs or OTC's which potentiate or depress (and indicate which effect) the therapeutic effects of this drug.

37. List any laboratory tests with which this drug interferes.

LONG TERM USAGE EFFECTS

38. Does this drug produce: Physical dependence _____, Psychological dependence ____, Tolerance ______?

39. List the signs and symptoms of cumulative toxicity.

Reference Number

40. List precautions.

41. Indicate if drug is teratogenic_____, mutagenic______, carcinogenic______.

THERAPEUTIC EFFICACY

42. Attach a bibliography of well controlled clinical studies with this drug.

43. List the therapeutic advantages of this drug over those in current use.

44. List its therapeutic disadvantages.

45. Attach some of the promotional literature and an evaluation of it.

POISON CONTROL INFORMATION

46. List signs and symptoms of overdose.

Reference number

47. List all antidotes (antagonists) in order of preference.

48. Outline the treatment of overdose.

49. Maximum ingested dose with recovery   Age of Patient

50. Toxic Serum Level ____ mg%; Lethal Serum Level _____ mg%

51. Attach procedure for quantitative determination of drug and its metabolites in blood and urine.

52. List dangerous combinations with this drug in overdosages.

ADMINISTRATION

53. List methods of administration

54. List any special techniques and equipment required for administration.

Reference Number

55. List professional instructions.

56. List patient instructions.

SUPPLY

57. (a) List all of the available dosage forms, strengths, and costs.

Proprietary Name	Manufacturer	Dosage Form	Strength	Retail Cost	Hospita Cost

ference
Number

57.(b). List the products containing this drug in combination with other drugs.

Proprietary Name	Manufacturer	Other Constituents

58. Comment on the effect of the various dosage formulations on the bio-availability of this drug.

Reference Number

SOLID ORAL DOSAGE FORMS

59. POSOLOGY:

	Recommended Oral Dose	Frequency (g. h.)	a.c. or p.c.	Period required for effect	Max.Duration of treatmt.	Primary Indicat
Adults						
Children						
Infants						

60. DESCRIPTION

Tablet____; Capsule____: hard___ soft____; Spheres ____

Uncoated____ Coated____: If Coated, specify kind of coatings:

S.C.____, E.C.____, FILM____, Sustained Release____

Size: Diameter____, Length____, Thickness____

Shape: Round____, Concave____, Convex____, Flat face____, Other_____.

Color___________;

Edges Bevelled: Yes____, No _____

Scored: Yes____, No_____.

Markings: Yes____, No_____; Indicate the type of marking______

61. List the names and amounts of all ingredients:

62. State the caloric content of the product.

eference
Number

63. Disintegration Time _____ min., State Standard.

64. Dissolution Rate ________. State name of method used.

65. To what extent is the drug soluble in:

a) Gastric Juice _______% soluble
b) Intestinal Juice ________% soluble

66. STABILITY

Dosage Form	Storeage Requirements	Shelf Life

67. Indicate the safety of the decomposition products:

NON-SOLID ORAL DOSAGE FORMS

68. Type of product: solution_____, suspension____, emulsion______.

69. Strength of product:

70. pH of product ________

71. List the names and amounts of all the ingredients:

Reference Number

72. Indicate any possible allergenic constituents:

73. Flavour of the product:

74. STABILITY:

Dosage Form	Storage Requirements	Shelf Life

75. List signs of deterioration:

76. List the decomposition products and indicate their safety:

77. POSOLOGY:

	Recommended Oral Dose	Frequency (q. h.)	a.c. or p.c.	Period required for effect	Max.Duration of treatment	Primary Indication
Adults						
Children						
Infants						

eference
Number

PARENTERAL DOSAGE FORMS

78. Type of Product: Solution_____, Suspension_____, Emulsion______, Lyophylized Powder_______, Other_______.

79. Route of administration: I.V.____, I.M.____, S.C._____, Intracutaneous_____, Intrathecal_____, Intraperitoneal________, Infusion_____, Other_____.

80. POSOLOGY:

	Recommended Dose	Frequency (q. H.)	a.c. or p.c.	Period required for effect	Max.Duration of treatmt.	Primary Indication
dults						
hildren						
nfants						

81. Incidence of pain and irritancy on injection and methods of minimizing these:

82. List the names and concentrations of all ingredients:

83. Vehicle(s): Water_____, Alcohol_____, Other______.

84. List preservative(s) and concentration(s).

85. List any possible allergenic constituents.

86. Is the product isotonic____, hypotonic_____, hypertonic_____

87. Agent(s) used to produce isotonicity:

Reference Number

88. pH of product _______

89. Viscosity of product _______

90. Coloring agent(s)

91. Can this product be re-autoclaved? Yes____, No____.

92. If "Yes" in (90), state conditions of re-autoclaving:

93. List signs of deterioration.

94. List the decomposition products and indicate their safety:

STABILITY

95. Dosage Form Storage Requirements Shelf Life

ADMINISTRATION

96. Is dilution necessary prior to administration?

Yes_____, No______

97. If "Yes" in (95) to what volume? ___________

ference
Number

98. If the product is lyophylized, state reconstitution directions:

99. Indicate the recommended infusion rate if the product is infused or administered by IV drip:

100. Provide where possible data on the utilization of this drug, i.e. frequency of use for a certain condition, comparison of use with other similar agents, etc.

ference
Number

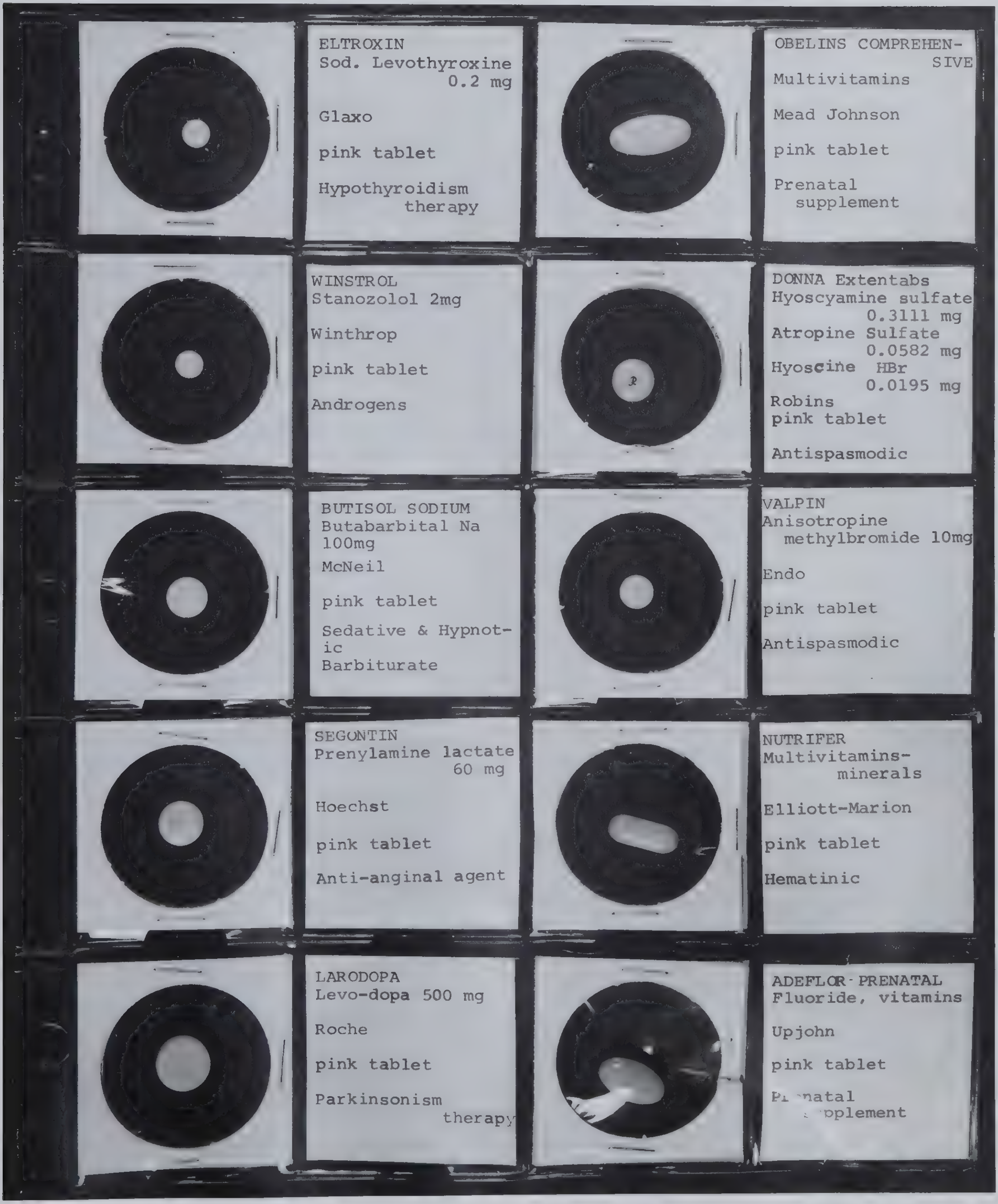
101. Provide information on physical and/or chemical incompatibilities (or attach an incompatibility table) when this drug is combined with others: (i.e., Normal Saline, Dextrose 5% in Water, Invert Sugar 5% or 10% in Water or Saline, etc.)

Name of Drug Added	Proprietary Name and Manufacturer	Quantity of this Drug	Quantity of other Drug Added	Vehicle	Nature of Incompatibility	Phys.Sign(s) of Incompatibility	Stability

APPENDIX II

SOLID DOSAGE FORM IDENTIFICATION SYSTEM

(CLASSIFICATION BY COLOR)



ELTROXIN
Sod. Levothyroxine
0.2 mg

Glaxo

pink tablet

Hypothyroidism
therapy

OBELINS COMPREHENSIVE
Multivitamins

Mead Johnson

pink tablet

Prenatal
supplement

WINSTROL
Stanozolol 2mg

Winthrop

pink tablet

Androgens

DONNA Extentabs
Hyoscyamine sulfate
0.3111 mg
Atropine Sulfate
0.0582 mg
Hyoscine HBr
0.0195 mg
Robins
pink tablet

Antispasmodic

BUTISOL SODIUM
Butabarbital Na
100mg
McNeil

pink tablet

Sedative & Hypnotic
Barbiturate

VALPIN
Anisotropine
methylbromide 10mg

Endo

pink tablet

Antispasmodic

SEGONTIN
Prenylamine lactate
60 mg

Hoechst

pink tablet

Anti-anginal agent

NUTRIFER
Multivitamins-
minerals

Elliott-Marion

pink tablet

Hematinic

LARODOPA
Levo-dopa 500 mg

Roche

pink tablet

Parkinsonism
therapy

ADEFLOR-PRENATAL
Fluoride, vitamins

Upjohn

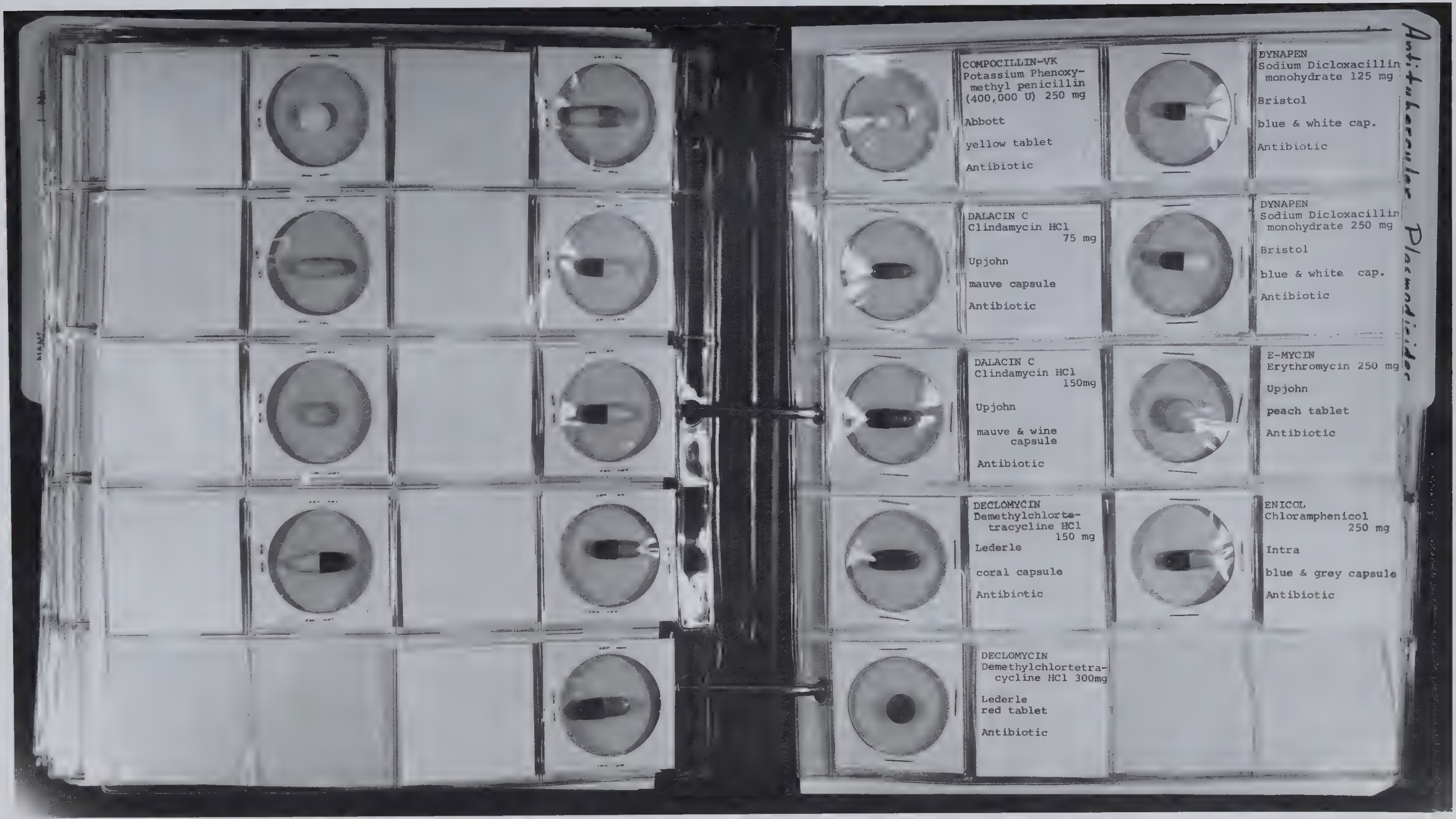
pink tablet

Prenatal
supplement

APPENDIX III

SOLID DOSAGE FORM IDENTIFICATION SYSTEM IN NOTEBOOK

(PHARMACOLOGIC-THERAPEUTIC CLASSIFICATION)



DYNAPEN
Sodium Dicloxacillin monohydrate 125 mg
Bristol
blue & white cap.
Antibiotic

COMPOCILLIN-VK
Potassium Phenoxymethyl penicillin (400,000 U) 250 mg
Abbott
yellow tablet
Antibiotic

DYNAPEN
Sodium Dicloxacillin monohydrate 250 mg
Bristol
blue & white cap.
Antibiotic

DALACIN C
Clindamycin HCl 75 mg
Upjohn
mauve capsule
Antibiotic

E-MYCIN
Erythromycin 250 mg
Upjohn
peach tablet
Antibiotic

DALACIN C
Clindamycin HCl 150mg
Upjohn
mauve & wine capsule
Antibiotic

ENICOL
Chloramphenicol 250 mg
Intra
blue & grey capsule
Antibiotic

DECLOMYCIN
Demethylchlortetracycline HCl 150 mg
Lederle
coral capsule
Antibiotic

DECLOMYCIN
Demethylchlortetracycline HCl 300mg
Lederle
red tablet
Antibiotic

APPENDIX IV

MEDICATION HISTORY

NAME:
SEX: __M, __F WEIGHT DATE OF BIRTH: MO__,DAY__, YR__
RACIAL ORIGIN: __Caucasian, __ Negro, __ Oriental, __ American Indian, __ Other
OCCUPATION:

---

1. CURRENT MEDICATIONS:

A. List all of the drugs and/or prescription numbers of drugs that you are taking at present or have taken in the past 6 months (including birth control pills).

	Medication	Prescription Number	Doctor	Name of Drug	Disorder or Reason for Taking drug	Drug Form	Daily Dose	Date Started	Do you take it regularly?
1.									
2.									
3.									
4.									
5.									
6.									

B. List the names of all the medications and any home remedies which you purchase and use frequently without a prescription.

Laxatives:
Antacids:
Analgesics:
Cold Preparations:
Antidiarrheals:

Vitamins:
Eye,Ear,Nose,Throat Preparations:
Allergy Preparations:
External Preparations:
(ointments, liniments, etc.)
Others

C. Do you use Alcohol __yes __no
Tobacco __yes __no

D. List any toxic agents (household chemicals, agricultural or industrial chemicals, pesticides, herbicides, etc.) to which you have been exposed in the past.

---

2. PAST MEDICATIONS:
Check any of the following which you may have had in the past 12 months.

Blood Transfusion __yes, __no
Anesthetic __yes, __no
Diagnostic Procedure __yes, __no Type______________________
Surgery __yes, __no Type______________________
Immunization __yes, __no
Medications administered to you in the doctor's office __yes, __no What?__________

B. List all medication that you have used in the past 12 months.

Medication	Prescription Number	Doctor	Name of Drug-store	Disorder or Reason for taking drug	Drug Form	Daily Dose	Date Started	Date Fin-ished	*Reason for discontinuing
1.									
2.									
3.									

3. Check any of the following to which you are allergic.

Penicillin __
Sulfas __
Aspirin __
Sleeping Pills __
Narcotics __
Antibiotics __

Iodine __
Horse Serum __
X-Ray Media __
Chocolate __
Fowl or Ducks __
Others __

B. List any drugs with which you have experienced any unpleasant side effects.
1.
2.

4. List any chronic illnesses or complaints which you may have.

APPENDIX V

DRUG INFORMATION

Review of a Patient - a 69 year old female diabetic.

Prothrombin Times were maintained at 20-28% until October 9.

No Prothrombin Times were available from October 10-12.

On October 13	Prothrombin Time was	56%
October 14	" " "	59%
October 16	" " "	46%

Changes in Medications:

October 8: NegGram 500 mg four times daily was started for U.T.I. Gantrisin 1 Gram every 12 hours was discontinued.

October 14: Tolbutamide was increased from 500 mg daily to 500 mgm twice daily.

October 13: Coumadin was increased from 1.25 mg daily to 2.5 mg daily.

In vitro studies conducted show that ethacrynic acid, mefenamic acid, nalidixic acid, and diazoxide can displace warfarin and other coumarin anticoagulants from plasma protein and thereby potentiate anticoagulation. If this effect occurs in vivo, clinical use of these drugs could cause an increase of 66-400% in free active anticoagulant and make it necessary to reduce anticoagulant dosage in order to prevent excessive hypoprothrombinemia and hemorrhage.
(Clin-Alrt, Aug. 14, 1970)

In the in vitro study a dose equivalent to 2-4 Grams of nalidixic acid per day caused an estimated increase of 64-160% in free warfarin concentration.

Nalidixic acid is excreted largely by the kidney and in the event of renal insufficiency very high plasma levels might be reached and warfarin activity would be increased.
(Clin Pharmacol Ther 11:524 (July-August) 1970)

Tolbutamide competes with warfarin for degradation sites in the endoplasmic reticulum of the liver.
(Deykin D., "Warfarin Therapy", New Eng J Med, 283:801-803).

In view of this evidence an increased sensitivity to warfarin is logically suspected; however, a decreased sensitivity to warfarin was manifested by this patient -- prothrombin activity increased from approximately 25 to 50% during treatment with nalidixic acid.

No explanation can be offered for this paradoxical situation. However, the relationship between warfarin and nalidixic acid and possibly tolbutamide is more complicated in vivo than in vitro.

APPENDIX V

SIDE EFFECTS OF LITHIUM CARBONATE

Most Common ones: slight tremor and polyuria

With higher doses or decreased excretion: nausea, vomiting and diarrhea

Gastro-Intestinal Symptoms:
- Anorexia
- Nausea
- Vomiting
- Diarrhea
- Thirst
- Dryness of the Mouth
- Weight Loss

Neuro-Muscular Symptoms & Signs:
- General muscle weakness
- Ataxia
- Tremor
- Muscle Hyperirritability:
  - Fasciculation
  - Twitching
  - Clonic movements of whole limbs
- Chorea-athetotic movements
- Hyperactive deep tendon reflexes

C.N.S.
- Anesthesia of skin
- Incontinuence of urine and feces
- Slurred speech
- Blurring of vision
- Dizziness
- Vertigo
- Epileptiform seizures

Mental Symptoms:
- Mental retardation
- Somnolence
- Confusion
- Restlessness--disturbed behavior
- Stupor
- Coma

Cardio-Vascular System
- Pulse irregularities
- Fall in blood pressure
- E.C.G. changes
- Peripheral circulatory failure
- Circulatory collapse

Miscellaneous

- Polyuria
- Glycosuria
- Lethargy and tendency to sleep
- Dehydration

References:

1. Noyes, R., Lithium Carbonate, Dis. Nerv. Syst., 30:318-21, (May 69).

2. Medical Letter, 12:10-11, Feb. 6, 1970.

APPENDIX VI

"ALICE'S PHARMACOLOGICAL ODYSSEY"

SLIDES	AUDIO
1. Title	
2. by etc.	
3. narrated by	
4. picture of history of drugs	The history of drug usage is long.
5. picture: 2-edged sword	Since the time drugs were introduced into medicine they have been known to help as well as harm patients.
6. arrow vs. elephant	Most past preparations have been weak and their side reactions mild,
7. bomb vs mouse	but present synthesized medications can cause a variety of severe adverse reactions:
8. grave yard	some have been fatal.
9. math equation	Many adverse effects are predictable from known pharmacological properties,
10. Einstein scratching head	but unpredictable reactions arise because the patient's response has little to do with the drug's main pharmacological action.
11. multiple drugs	Knowing that drugs are potentially hazardous and faced with the multiplicity of preparations it is little wonder that the clinician considers drug-induced diseases a problem. To illustrate some factors in this problem, a few drugs will be presented in various situations. Some of these drugs are no longer on the market and some are rarely used. However, they are included merely as examples of toxicities.

SLIDES	AUDIO
12. little baby	These drugs will be given to Alice.
13. pregnant mother	Alice's drug saga began before she was born. In the 6th month of pregnancy with Alice, her mother developed a urinary tract infection due to E. coli.
14. E coli and tetracycline prescription	The infection was treated with tetracycline.
15. yellow teeth	When Alice's teeth began to erupt at expected times, all of her teeth were discolored a yellowish-brown and showed some hypoplasia.
16. mechanism	The pigmentation is due to the tetracycline chelating calcium, and this is incorporated into tissue undergoing calcification as a tetracycline-calcium-orthophosphate complex.
17. normal girl	Alice developed normally and had the occasional sore throat which always responded to penicillin treatment.
18. sore throat and penicillin prescription	During the winter of her 8th year, Alice developed another sore throat. Suspecting a streptococcal infection, her doctor administered IM penicillin.
19. calamity	Within minutes, Alice developed an anaphyllactic reaction--a rare occurrence--
20. rash	complete with an erythematous rash.
21. mechanism	From her previous penicillin therapy, Alice had become sensitized. Penicilloyl, one of the degradation products of penicillin metabolism, combines with protein to form an antigen, which stimulates antibody production.

SLIDES	AUDIO
22. mechanism	When re-challenged with penicillin antigen,an antigen-antibody reaction occurs, producing histamine release and resulting in the dangerous anaphyllaxis. Alice was successfully treated with adrenalin and supportive therapy.
23. shy girl	In her teens, Alice was a shy obese girl.
24. diet	She dieted with low calorie products, containing cyclamates which were subsequently banned because they produced urinary bladder carcinomas in rats and mice.
25. lasting friend	Poor Alice continued to grow plump and became severely depressed. Several anti-depressants were tried but Parnate seemed most effective.
26. mechanism	One route of matabolism of monamines, such as adrenalin and tyramine, is by monamine oxidase. Parnate irreversibly inactivates this enzyme.
27. mechanism	Consequently, an accumulation of vasopressor agents occurs.
28. wine and cheese	Alice went to a wine and cheese party and forgot the warning to avoid such tyramine-containing products.
29. emergency	She arrived in emergency with an excruciating occipital headache, was diagnosed as having a hypertensive crisis, and was effectively treated with sodium nitroprusside.
30. pregnant woman	One day Alice married and soon she was expecting her first child.

SLIDES	AUDIO
31. thalidomide	During the first trimester, Alice had trouble sleeping. Thalidomide was prescribed.
32. phocomelia	Alice's baby was born with phocomelia -- seal flipper limbs.
33. phocomelia	Thalidomide was withdrawn from all drug markets but not before more deformed babies were born.
34. pills plus headache	For years now, Alice had been troubled with headaches which she had self-treated with a preparation containing aspirin, phenacetin, and caffeine. This preparation could be obtained without a prescription.
35. kidney -- diseased	Later, Alice read that the ingestion of phenacetin could cause nephrotoxicity,
36. aspirin	so she changed to plain aspirin.
37. stomach ache	Occasionally she experienced some gastrointestinal discomfort and pain, and so continued to treat herself with more aspirin.
38. family	When Alice's family was complete,
39. pill and headache etc.	she was put on the pill--one containing high levels of estrogen. Her headaches became more frequent and one day she experienced severe calf pain. The diagnosis of deep vein thrombosis was made upon hospitilization.
40. graph of anticoagulants	The birth control pills were discontinued and anti-coagulant therapy was initiated using first heparin then coumarin... She recovered and was sent home on coumarin.

SLIDES	AUDIO
41. Bayers works Wonders	At home, Alice resumed aspirin therapy for her epigastric pain and the following day was brought to emergency in shock.
42. gastric ulcer	She had hemorrhaged from a reactivated gastric ulcer. This was caused by the irritant aspirin and aggravated by the anticoagulated blood.
43. coumarin given the boot	In the blood, coumarin is protein-bound. Acetylsalicylic acid displaces the coumarin, increases the levels of free coumarin and thereby enhances the anticoagulant effect. Again Alice was successfully treated.
44. Rheumatoid Arthritis	Shortly after Alice celebrated her 35th birthday, she complained of weight loss, malaise, and severe joint pain. She had rheumatoid arthritis.
45. graph	She was started on high doses of enteric-coated aspirin but her disease did not respond and she was subsequently tried on prednisone. As the attack subsided, steroid levels were reduced but attempts to completely eliminate the prednisone were unsuccessful.
46. picture: Cushingoid woman (Netter's)	As time passed hypercortisonism appeared, featuring red cheeks, buffalo hump, moon face, thin skin, ecchymosis, thin arms and legs, red striae, pendulous abdomen, poor wound healing and osteoporosis.
47. ankle edema	Mild hypertension and ankle edema developed which were treated with hydrochlorthiazide, a potassium depleting diuretic.

SLIDES	AUDIO
48. X-ray of chest	Later Alice began to display evidence of left ventricular failure. Digitalis and potassium chloride were prescribed. She immediately stopped taking the potassium chloride because of its bad taste.
49. drawing of kidney tubule	A short while later Alice returned to her doctor complaining of nausea, visual disturbances, muscle weakness, and tachycardia.
50. ECG	Digitalis toxicity and hypokalemia were detected on her electrocardiogram. Alice responded to treatment.
51. shadow of woman	Alice's saga illustrates some manifestations of drug-induced diseases such as congenital anomalies, metabolic derangements, endocrinopathies, and immunological reactions.
52. table: ingestion to excretion	Some side reactions are predictable when one considers the ingestion, action, metabloism, and excretion of a drug.
53. overdosage	Too much of any drug can be harmful.
54. Action	A drug may act undesirably on multiple systems. A Timely example is l-Dopa.
55. metabolism	Enzymes necessary for drug metabolism may be deficient as seen in very young and very old people, in inherited deficiencies, and in starvation states.
56. excretion	And excretion may be hampered through concurrent liver or kidney disease. A number of other factors are also important.

SLIDES	AUDIO
57. sex	Women are thought to experience untoward effects from drugs more frequently than men.
58. allergies	Patients with allergies develop adverse reactions to drugs more often,
59. avoid multiple drugs	and multiple drug therapy increases the likelihood of adverse reactions through interference or from a combination of effects.
60. balance	Rational drug therapy demands that the potential benefits of drugs must be weighed against their potential risks.

APPENDIX VII

HOSPITAL B

APPLICATION FOR ADMISSION

Medicine ☐ Surgery ☐ EENT ☐ GYN ☐ UROL ☐ OBS ☐ ORTHO ☐ HISTORY ☐ PAED ☐ PSYCH ☐

Sex M. ☐ F. ☐

Attending Doctor: ____ M.D.

Responsible for History

Surgeon/Consultant: ____ M.D.

Assistant Surgeon: ____ M.D.

Referring Doctor: ____ M.D.

Drug Allergies:

PATIENT'S NAME ____ Age ____ Yrs.

ADDRESS ____ Home Phone ____

____ Business Phone ____

DIAGNOSIS ____

OPERATION ____

ANAESTHETIC: General ☐ Local ☐ Pre-Op Physio ☐ Yes ☐ No ☐

Time to complete ____ hrs. **BLOOD** Amount required ____ c.c.X (Available in 20 mins.) ____ c.c.Y. (Ready for Surgery)

RECENT MEDICATION:
Antihypertensive ☐ Digitalis ☐
Cortisone ☐ Insulin ☐
Tranquilizers ☐
Other

Type of accommodation required: Semi ☐ Priv. ☐ Std. ☐

Disposition of Patient on Discharge:
Home ☐ Activitation ☐
Nursing Home ☐ Other ____

Social Service Department notified? Yes ☐ No ☐

Additional Information affecting date and time of admission: ____

ADMITTING ORDERS

Doctor's instructions to Nursing Unit, Operating Room, etc: ____

PHYSIOTHERAPY ☐

Pharmacy

℞ ____

Laboratory

Radiology

O.R. PRIORITIES

MONTHS	1/2	1	2	3	4	5	6	7	8
MAJOR									
MINOR									

PREDICTED LENGTH OF STAY ☐ DAYS

Admitted ____ 196 ____

Patient Number ____ Room & Bed ____

Physician's Signature ____ M.D.

Date ____ 196 ____

REVALIDATIONS:

1. Signed ____ Date ____ 196 __
2. Signed ____ Date ____ 196 __
3. Signed ____ Date ____ 196 __

APPENDIX VIII

LITERATURE EVALUATION

1. Title:

2. Author:
   Independent or Supported Study:

3. Disease or Pathogen treated:

4. Coexisting Diseases:

5. Interacting Agents:

6. Other Agents Co-Administered:

7. Effect observed in: Humans:____, Animals:____, In Vitro:____,
   Extrapolated from related drugs:_____.

8. Nature of Interaction: Increased therapeutic effect________,
   Decreased effect______, Increased adverse effects______,
   Other______

9. Proposed mechanism of interaction:

10. Frequency of observed interaction: in article:____________
    Other references:________

11. Statistical characterization of data:

12. Route of Administration--Penicillin_________, Interactant_______.

13. Dosage form--Penicillin________, Interactant_________.

14. Size of Dose--Penicillin____________________, Interactant_________.

15. Frequency of Dose--Penicillin________________, Interactant________

16. Other Host Information of relevant of available:
    Age:
    Sex:
    Race:
    Occupation:
    Habits:
    Kidney Function:
    Liver Function:
    Chronic Disease:
    pH U.T., G.I.T.:

17. Valid Article or Invalid Article

APPENDIX IX

MEDICAL RECORDS SURVEY

1. Patient Hospital number ____________ Age _____
Sex ____________ Weight ____________ Race ____________
(Occupation ________________)

2. Reason for Penicillin therapy:

3. Concurrent condition(s)

4. Penicillin G used: Potassium, Sodium

5. Dosage Form ________________ Route of administration ______
Size of Dose ________________
Frequency of Dose ____________ Time(s) of administration ____

6. Other Concurrent Drugs (checked if coadministered; circled if potential interactants).

6a. Indicate Dosage form, Route, Size of dose, frequency and time of administration of interactant.

7. Indicate if any evidence of interaction.

8. Indicate if "interaction" is of any clinical significance.

9. List other penicillin or antibiotic used subsequently:

10. Any ADR

APPENDIX X

PENICILLIN G ADMINISTRATION

Patient's Name:

Please chart exact time that mid-day and evening doses of Penicillin G were administered to this patient.

Day Date Time

(1) . . . .

(2) . . . .

(3) . . . .

(4) . . . .

(5) . . . .

Please return this sheet to when chart is complete or when the Penicillin G is discontinued.

Thank you.

APPENDIX XI
PROFILE

Weight______ Drug Hypersensitivities______________

Diagnosis______________________________

Impaired Functions: Kidney__ Liver__ Marrow__

DRUG	ROUTE	DOSAGE SCHEDULE	START	DISC	COMMENTS

DRUG-DRUG INTERACTIONS

UG	DRUG	EFFECT

DRUG HISTORY

DRUG	DOSAGE	DURATION

INITIATION TIME______________________

MAINTENANCE TIME______________________

____

____

____

OTHER TIME

LABORATORY DATA

E O.	LAB TEST	DATE D.	RESULTS

Cultures and Sensitivities

E O.	TYPE	DATE D.	ORGANISM	SENSITIVITY

Temperature

P						

DRUG-LAB TEST INTERACTIONS

DRUG	LAB TEST	EFFECT	DRUG	LAB TEST	EFFECT

Initiation Time ____________________ Other Time

Maintenance Time ____________________

____

____

____

BIBLIOGRAPHY

1. Francke, D.E., Can. J. Hosp. Pharm., 23, 185 (1970).
2. Report of the Committee on Curriculum, Am. J. Pharm. Ed., 32, 435 (1968).
3. Tyler, V.E., Am. J. Pharm. Ed., 32, 764 (1968).
4. Parks, L.M., Seminar on "Pharmacy in Transition", College of Pharmacy, University of Kentucky, (1968), p. 40.
5. Durgin, Sister Jane Marie, Hosp. Topics, 49, 61 (1971).
6. Bouchard, V.E., Drug Intell. Clin. Pharm., 3, 342 (1969)
7. Slining, J., Cole, P., and Sister Emmanuel, Am. J. Hosp. Pharm., 27 459 (1970).
8. Moynaham, P.M., Drug Info. Bull., 4, 43 (1970).
9. Francke, D.E., Am. J. Hosp. Pharm., 19, 359 (1962).
10. Smith, W.E., O'Malley, C.D. and Weiblen, J.W., Hospitals, 44, 88 (1970).
11. Owyang, E., Miller, R.A., and Brodie, D.C., Am. J. Hosp. Pharm., 25, 624 (1968).
12. Bell, J.E., Grimes, B.J., Bouchard, V.E., and Duffy, Sister M. Gonzales, Am. J. Hosp. Pharm., 27, 29 (1970).
13. Burkholder, D., Drug Intell., 3, 69 (1969).
14. Hassan, W.E., "Hospital Pharmacy", 2nd Ed., Lea and Febiger, Philadelphia, 1967, p. 315.
15. Rosenberg, J.M., and Peritore S.P., Am. J. Hosp. Pharm., 28, 270 (1971).
16. de Haen, P., Am. J. Hosp. Pharm., 23, 71 (1966).
17. Burkholder, D., Am. J. Hosp. Pharm., 20, 506 (1963).
18. Anderson, R.D., and Latiolais, C.J., Am. J. Hosp. Pharm., 22, 53 (1965).
19. Burkholder, D., Am. J. Hosp. Pharm., 24, 216 (1967).
20. Reilly, Mary Jo, Am. J. Hosp. Pharm., 25, 587 (1968).
21. Hospital Pharmacists Seminar, Public Health Report, 80, 603 (1965).

22. Humphrey, H., Am. J. Hosp. Pharm., 22, 4 (1965).

23. Mahon, W.A., and Daniel, E.E., Can. Med. Assoc. J., 90, 565 (1964).

24. Lasagna, L., ed., "Clinical Pharmacology", Vol. I and II, 1st Ed., Pergamon Press, Toronto, 1966.

25. Wilson, G.M., Br. Med. J., 1, 1065 (1966).

26. Jarvik, M.E., in "The Pharmacological Basis of Therapeutics", 4th Ed., edited by Goodman, L.S., and Gilman, A., Macmillan, New York, 1970, p. 166.

27. Danowski, T.S., Bonessi, J.V., Sabeh, G., Sutton, R.D., Webster, M.W., and Sarver, M.E., Ann. Intern. Med., 61, 11 (1964).

28. Newman, S., in "Diseases of Medical Progress: A Study of Iatrogenic Disease", 3rd Ed., Edited by Moser, R.H., Charles C. Thomas, Springfield, Illinois, 1969, p. 372.

29. Mills, D.H., Calif. Med., 101, 4 (1964).

30. Hutchinson, R.A., Hosp. Pharm., 3, 20 (1968).

31. Lesshafft, C.T., Jr., J. Am. Ph. Assoc., NS10, 205 (1970).

32. McCarron, M., "An Approach to the Education of Patient-Oriented Pharmacists", copyright privileges of the American Association of Colleges of Pharmacy, Silver Spring, Maryland.

33. McHale, M.K. and Canada, A.T., Drug Intell., 3, 155 (1969).

34. McLean, W.M., Bohl, J.C., Scott, W.V., Meyer, F., Thudium, V.F., and Phillips, G.L., Am. J. Hosp. Pharm., 26, 399 (1969).

35. Fortner, C.L., Voices 12/60, Vol. 1, No. 4, (1971).

36. Emmanuel, Sister, Hosp. Manage., 109, 44 (1970).

37. Covington, T.R., and Whitney, H.A.K., "Patient-Pharmacist Communication Techniques", Paper presented at 5th Annual Midyear Clinical Meeting of the American Society of Hospital Pharmacists, Anahein, Calif., Dec., 1970.

38. Wilson, R.S., and Kabat, H.F., Am. J. Hosp. Pharm., 28, 49 (1971).

39. Hefferren, J.J., J.A.M.A., 182, 1145 (1962).

40. Gupta, R.C. and Kofoed, J., "Identification Guide for Tablets and Capsules", Canada Law Book Company Ltd., Toronto, 1967.

41. Wood, K., Jr., Am. J. Hosp. Pharm., 26, 701 (1969).

42. Flood, A.J., Hospitals, 45, 72 (1971).

43. Smith, D.L., Can. J. Hosp. Pharm., 23, 191 (1970).

44. Shilling, J.G., J. Am. Pharm. Assoc., NS6, 632 (1966).

45. Gibson, M.R., J. Am. Pharm. Assoc., NS6, 632 (1966).

46. Fox, L.A., Am. J. Hosp. Pharm., 26, 334, (1969).

47. Brand, A.J., J. Am. Pharm. Assoc., NS7, 634, (1967).

48. deLeon, R.F., J. Am. Pharm. Assoc., NS11, 54 (1971).

49. Friend, D.G., J. Am. Pharm. Assoc., NS4, 528 (1964).

50. Latiolais, C.J. and Berry, C.C., Drug Intell. Clin. Pharm., 3, 270 (1969).

51. Malahy, B., Am. J. Hosp. Pharm., 23, 283 (1966).

52. Clinite, J.C., and Kabat, H.F., J. Am. Pharm. Assoc., NS9, 450 (1969).

53. Gelber, I., "Released Mental Patients on Tranquilizing Drugs and the Public Health Nurse", University Press, New York, 1959.

54. Silnutzer, A., Pharm. Times, 36, 44 (1970).

55. Bellafiore, I.J., J. Am Pharm. Ed., 38, 85 (1971).

56. Hynniman, C.E. and Lamy, P.P., J. Am. Pharm. Assoc., NS11, 158 (1971).

57. Falconer, M., Can Pharm. J., 104, 148 (1971).

58. Cockerham, M.F., Hospitals, 44, 57 (1970).

59. Bowles, G.C., Mod. Hosp., 114, 130 (1970).

60. Ligon, M., Can.Pharm. J., 104, 68 (1971).

61. U.S. Department of Health, Education and Welfare Task Force on Prescription Drugs, "The Drug Prescribers", U.S. Government Printing Office, Washington, D.C. 1969, p.21.

62. U.S. Department of Health, Education and Welfare Task Force on Prescription Drugs, "The Drug Prescribers", U.S. Government Printing Office, Washington, D.C. 1969, p. 3.

63. Stolley, P.D., and Lasagna, L., J. Chron. Dis., 22, 395 (1969).

64. Ogilvie, R.I. and Ruedy, J., Can. Med. Assoc. J., 97, 1450 (1967).

65. Winnick, C., Sociometry, 24, 384 (1961).

66. Williamson, R.E., and Kabat, H.F., J. Am. Pharm. Assoc., NS11, 164 (1971).

67. Henley, S., Tester, W.W., Knapp, R., Hospitals, 42, 99 (1968).

68. U.S. Department of Health, Education, and Welfare Task Force on Prescription Drugs, U.S. Government Printing Office, Washington, D.C., 1968, p. 54.

69. Walton, C.A., Drug Intell., 1, 133 (1967).

70. Hirschman, J.L., and Maudlin, R.K., Drug Intell. Clin. Pharm., 4, 10 (1970).

71. Stevens, K.M., Voices 12/60, Vol. 1, No. 1, (1971).

72. Cain, R.M., Drug Intell. Clin. Pharm., 4, 38, (1970).

73. Thompson, C.O., Schwartu, N.W., Trites, D.K., and Leckwart, J.F., Am. J. Hosp. Pharm., 27, 277 (1970).

74. Levine, M.E., Am. J. Hosp. Pharm., 27, 294 (1970).

75. Barbeau, A., Can. Med. Assoc. J., 101, 791 (1969).

76. Morgan, J.P., and Bianchine, J.R., Rational Drug Ther., 5:1 (1971).

77. Brodie, D.C., "The Challenge to Pharmacy in Times of Change", Commission on Pharmaceutical Services to Ambulant Patients by Hospital and Related Facilities, American Pharmaceutical Association, 1966, p. 39.

78. Francke, D.E., Drug Intell., 1, 243 (1967).

79. Smith, W.E., Drug Intell. Clin. Pharm., 3, 322 (1969).

80. Hassan, W.E., "Hospital Pharmacy", 2nd Ed., Lea and Fibiger, Philadelphia, 1967, p. 83.

81. Lucille, Sister M. and Rappaport J., Hospitals, 43, 74 (1969).

82. Benson, S.B., and Kabat, H.F., Am. J. Hosp. Pharm., 24, 263 (1967).

83. Greth, P.A., Tester, W.W., and Black, H.J., Am. J. Hosp. Pharm., 22, 558 (1965).

84. Mahoney, R.W., Hospitals, 40, 138 (1966).

85. Barker, K.N., and Heller, W.M., Am. J. Hosp. Pharm., 20, 568 (1963).

86. Prisco, H.M., and Plein, E., Am. J. Hosp. Pharm., 26, 160 (1969).

87. "Audiovisual Aids in Modern Medical Education", Documenta Geigy, (1968), p. 1.

88. Zilz, D.A., Drug Intell., 3, 218 (1969).

89. Smith, W.E., Drug Intel. Clin. Pharm., 4, 73 (1970).

90. Ginsberg, M.P., and Birmingham, P.H., Hospitals, 44, 94 (1970).

91. Visconti, J.A., Am. J. Hosp. Pharm., 26, 378 (1969).

92. Morelli, H.F. and Melmon, K.L., Calif. Med., 109, 380 (1968).

93. Puckett, W.H., and Visconti J.A., Am. J. Hosp. Pharm., 28, 247 (1971).

94. Hartshorn, E.A., Drug Intell. Clin. Pharm., 4, 173 (1970).

95. Elking, Sister Mary Pualette and Kabat, H.F., Am. J. Hosp. Pharm., 25, 485 (1968).

96. Munzenberger, P., and Emmanuel, Sister, "The Incidence of Drug-Diagnostic Test Interference in Patients Treated on an Out-Patient Basis", Paper presented at 5th Annual Midyear Clinical Meeting of the American Society of Hospital Pharmacists, Anaheim, Calif., Dec., 1970.

97. Azarnoff, D.I., Pharmacol. for Physicians, 4, 1 (Feb. 1970).

98. Weinstein, L., in "The Pharmacological Basis of Therapeutics", 4th Ed., edited by Goodman, L.S., and Gilman, A., Macmillan, New York, 1970, p. 1256.

99. Jarvick, M.E. in "The Pharmacological Basis of Therapeutics", 4th Ed., edited by Goodman, L.S., and Gilman, A., Macmillan, New York, 1970, p. 185.

100. Editorial, New Eng. J. Med., 279, 1286 (1968).

101. Moser, R.H., New Eng. J. Med., 255, 606 (1956).

102. Melmon, K.L., New Eng. J. Med., 284, 1361 (1971).

103. Seidl, L.G., Thornton, G.F., Smith, J.W., and Cluff, L.E., Bull. Johns Hopkins Hosp., 119, 299 (1966).

104. Hoddinott, B.C., Gowdey, C.W., Coulter, W.K., and Parker, J.M., Can. Med. Assoc. J., 97, 1001 (1967).

105. Schimmel, E.M., Ann. Intern. Med., 60, 100 (1964).

106. Hurwitz, N., Br. Med. J., 1, 539 (1969).

107. U.S. Department of Health, Education, and Welfare Task Force on Prescription Drugs: Final Report, U.S. Government Printing Office, Washington, D.C., 1969.

108. Weston, Jean K., J.A.M.A., 203, 35 (1968).

109. Reidenberg, M.M., J.A.M.A., 203, 31 (1968).

110. MacDonald, M.G., and MacKay, B.R., J.A.M.A., 190, 1071 (1964).

111. Koch-Weser, J., Drug Info. Bull., 2, 72 (1968).

112. "International Drug Monitoring: the Role of the Hospital -- a WHO Report", Drug Intell. Clin. Pharm., 4, 101 (1970).

113. Parks, J.S., Can. J. Hosp. Pharm., 23, 147 (1970).

114. Jick, H., Miettinen, O.S., Shapiro, S., Lewis, G.P., Siskind, V., and Slone, D., J.A.M.A., 213, 1455 (1970).

115. Hynniman, C.E., Hosp. Pharm., 4, 9 (June 1969).

116. "Adverse Reactions Reporting Systems", Report on International Conference, Hospitals, 44, 80 (1970).

117. Philp, J.R., Am. J. Hosp. Pharm., 27, 659 (1970).

118. Brodie, D.C., Drug Intell. Clin. Pharm., 4, 203 (1970).

119. Burkholder, D.F., Drug Intell., 1, 87 (1967).

120. Bowles, G.C., Mod. Hosp., 114, (1970).

121. Sharpless, S.K., in "The Pharmacological Basis of Therapeutics", 4th Ed., edited by Goodman, L.S. and Gilman, A., Macmillan, New York, 1970, p. 112.

122. Barker, K., and McConnel, W., Am. J. Hosp. Pharm., 19, 360 (1962).

123. Barker, K., and Heller, W., Am. J. Hosp. Pharm., 21, 609 (1964).

124. Vere, D.W., Lancet, 1, 370 (1965).

125. Anderson, R.D., Am. J. Hosp. Pharm., 28, 18 (1971).

126. Shellenberg, R., "Causes and Controls of Medication Errors" unpublished paper submitted to Department of Hospital Administration in partial fulfilment of requirements for Diploma in Hospital Administration in School of Hygeine, University of Toronto, 1968.

127. Barker, K.N., Am. J. Hosp. Pharm., 26, 324 (1969).

128. Hynniman, C.E., Conrad, W.F., Urch, W.A., Reidnick, B.R., and Parker, P.F., Am. J. Hosp. Pharm., 27, 803 (1970).

129. Hartshorn, E.A., Drug Intell. Clin. Pharm., 4, 173 (1970).

130. Gant, B.G., and Waller, R.H., "Drug Interaction Index", Meditec Publications Ltd., Kelowna, B.C., Canada.

131. Hartshorn, E.A., "Handbook of Drug Interactions", Donald E. Francke, publisher, Cincinnati, Ohio, 1970.

132. Tuttle, C.B., Can. J. Hosp. Pharm., 22, 125 (1969).

133. Carson, J.A., "Drug Interaction Manual", Danville Pharmaceutical Publishing Co. Inc., Danville, Illinois, 1970.

134. Autian, J., Berman, A., and Guess, W.L., Am. J. Hosp. Pharm., 20, 467 (1963).

135. Weinstein, L., in "The Pharmacological Basis of Therapeutics", 4th Ed., edited by Goodman, L.S. and Gilman, A., Macmillan, New York, 1970, p. 1212.

136. McDermott, W., Bunn, P.A., Benet, M., Dubois, R., and Reynolds, M.E., J. Clin. Invest., 25, 190 (1946).

137. Fishman, L.S., and Hewitt, W.L., Med. Clin. N.A., 54, 1081 (1970).

138. Finland, M., Meads, M., and Ory, E.M., J.A.M.A., 129, 315 (1945).

139. Broh-Kahn, R.H., and Pedrick, R.F., Am. J. Med. Sci., 221, 691 (1946).

140. Markowitz, M., and Kuttner, A.G., J. Pediatrics, 31, 195 (1947).

141. Hewitt, W.L., Seligman, S.J., and Deigh, R.A., J. Lab. Clin. Med., 67, 792 (1966).

142. Jawetz, E., Gunnison, J.B., Coleman, V.R., Science, 111, 254 (1950).

143. Koenig, M.G., and Kaye, D., New Eng. J. Med., 264, 257 (1961).

144. Jawetz, E., and Sonne M., New Eng. J. Med., 274, 710 (1966).

145. Garrod, L.P., and Waterworth, P.M., J. Clin, Path., 15, 328 (1962).

146. Manten, A., and Terra, J., Chemotherapia, 8, 21 (1964).

147. Simon, C., Chemotherapia, 11, 43 (1966).

148. Jawetz, E., in "Annual Review of Pharmacology", edited by Elliot, H.W., Cutting, W.C., and Dreisbach, R.H., Annual Reviews Inc., Palo Alta, California, 1968, p. 159.

149. Jawetz, E., in "annual Review of Pharmacology", edited by Elliott, H.W., Cutting, W.C., and Dreisbach, R.H., Annual Reviews Inc., Palo Alta, California, 1968, p. 161.

150. Crofton, J., Br. Med. J., 2, 137 (1969).

151. Avakian, S. and Kabacoff, B.C., Clin. Pharmacol. Therap.m 5, 716 (1964).

152. Weinstein, L., in "The Pharmacological Basis of Therapeutics" 4th Ed., edited by Goodman, L.S., and Gilman, A., Macmillan, New York, 1970, p. 1219.

153. Sabath, L.D., Elder, H.A., McCall, C.E., and Finland, M., New Eng. J. Med., 277, 232 (1967).

154. Kunin, C.M., Clin. Pharmacol. Therap., 7, 180 (1966).

155. Kane, Gordon, "An Evaluation of the Significance of Some Penicillin-Laboratory Test Interactions", unpublished report submitted in partial fulfilment of the requirements of Pharmacy Residency Program, Vancouver, B.C., Canada, 1971.

156. Modell, W., Clin. Pharmacol. Therap., 5, 265 (1964).

157. Bunn, P.A., Pediatric Clin. N.A. 8, 981 (1961).

158. Fishman, L.S., and Hewitt, W.L., Med. Clin. N.A., 54, 1081 (1970).

159. Weinstein, L., in "The Pharmacological Basis of Therapeutics", 4th Ed., edited by Goodman, L.S., and Gilman, A., Macmillan, New York, 1970, p. 1219.

160. Medical Letter, 9, 55 (1967).

161. "Adverse Reactions Reporting Systems", Hospitals, 44, 80 (Dec. 16, 1970).

162. Emmanuel, Sister, and Dauphnais, R.J., Drug Intell., 2, 118 (1968).

163. Danielson, F., Hosp. Pharm., 5, 21 (1970).

164. Kabat, H.F., Can. J. Hosp. Pharm., 23, 196 (1970).

155. Kane, Gordon, "An Evaluation of the Significance of Some Penicillin-Laboratory Test Interactions", unpublished report submitted in partial fulfillment of the requirements of Pharmacy Residency Program, Vancouver, B.C., Canada, 1971.

156. Modell, W., Clin. Pharmacol. Therap., 5, 265 (1964).

157. Bunn, P.A., Pediatric Clin. N.A. 8, 981 (1961).

158. Fishman, L.S., and Hewitt, W.L., Med. Clin. N.A., 54, 1081 (1970).

159. Weinstein, L., in "The Pharmacological Basis of Therapeutics", 4th Ed., edited by Goodman, L.S., and Gilman, A., Macmillan, New York, 1970, p. 1219.

160. Medical Letter, 9, 55 (1967).

161. "Adverse Reactions Reporting Systems", Hospitals, 44, 80 (Dec. 16, 1970).

162. Emmanuel, Sister, and Dauphnais, R.J., Drug Intell., 2, 118 (1968).

163. Danielson, F., Hosp. Pharm., 5, 21 (1970).

164. Kabat, H.F., Can. J. Hosp. Pharm., 23, 196 (1970).